CDC Centers for Disease Control and Prevention

Opioid Overdose

Synthetic Opioid Overdose Data

In 2018, more than 31,000 deaths involving synthetic opioids (other than methadone) occurred in the United States, which is more deaths than from any other type of opioid. Synthetic opioid-involved death rates increased by 10% from 2017 to 2018 and accounted for 67% of opioid-involved deaths in 2018.

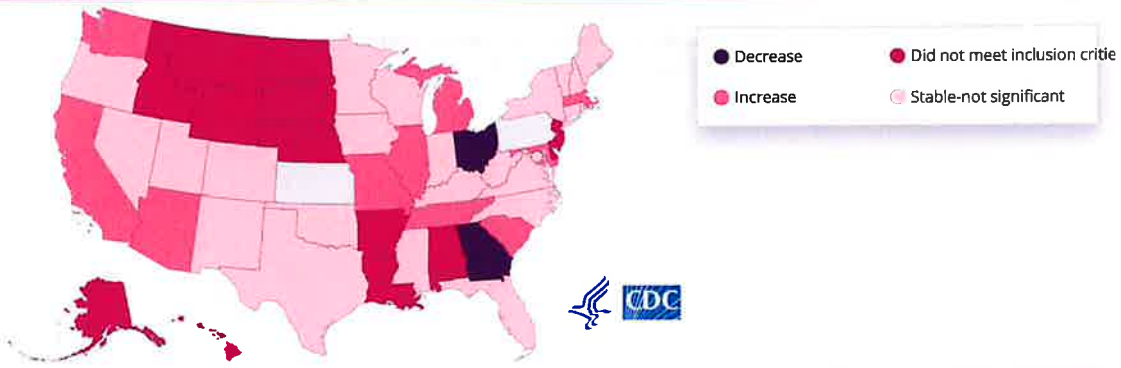
- Rates increased from 2017 to 2018 among males and females, persons 25 years and older, non-Hispanic whites, non-Hispanic blacks, Hispanics, non-Hispanic Asian/Pacific Islanders, and in large central metro, large fringe metro, medium metro, and small metro counties.
- Rates increased in the Northeast, South and West and remained stable in the Midwest.
- Rates increased in 10 states and decreased in two states. The largest relative increase occurred in Arizona (92.5%), and the largest absolute increase occurred in Maryland and Missouri (4.4 per 100,000 in both states); the largest relative and absolute decrease was in Ohio (-20.7%, -6.7 per 100,000). The highest synthetic opioid-involved death rate in 2018 occurred in West Virginia (34.0 per 100,000).[1]

Previous reports have indicated that increases in synthetic opioid-involved deaths have been associated with the number of drug submissions obtained by law enforcement that test positive for fentanyl but not with fentanyl prescribing rates. These reports indicate that increases in synthetic opioid-involved deaths are being driven by increases in fentanyl-involved overdose deaths, and the source of the fentanyl is more likely to be illicitly manufactured than pharmaceutical.[2,3,4]

There are also fentanyl analogs, such as acetylfentanyl, furanylfentanyl, and carfentanil, which are similar in chemical structure to fentanyl but not routinely detected because specialized toxicology testing is required. Recent surveillance has also identified other emerging synthetic opioids, like U-47700.[5] Estimates of the potency of fentanyl analogs vary from less potent than fentanyl to much more potent than fentanyl, but there is some uncertainty because potency of illicitly manufactured fentanyl analogs has not been evaluated in humans. Carfentanil, the most potent fentanyl analog detected in the U.S., is estimated to be 10,000 times more potent than morphine.[5,6]

2017–2018

Statistically significant changes in drug overdose death rates involving synthetic opioids by select states, United States, 2017 to 2018



Data Table +

SOURCE: CDC/NCHS, National Vital Statistics System, Mortality. CDC WONDER, Atlanta, GA: US Department of Health and Human Services, CDC; 2018. https://wonder.cdc.gov/

About This Map and Data Table +

2016–2017

About This Map and Data Table +

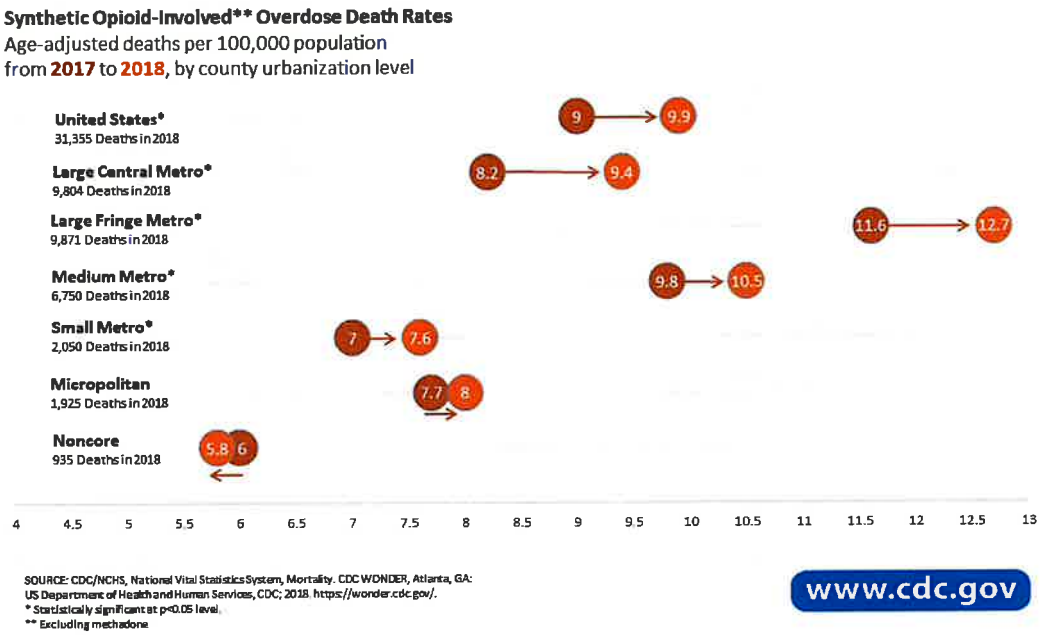
2017-2018 Urbanicity −

U.S. Synthetic Opioid Overdose Urbanicity

The figures below show the changes in age-adjusted death rates involving synthetic opioids by urbanization classification of residence from year to year.

- **Large central metro**—Counties in metropolitan statistical areas of 1 million or more population that:
  - Contain the entire population of the largest principal city
  - Have their entire population contained in the largest principal city
  - Contain at least 250,000 inhabitants of any principal city
- **Large fringe metro**—Counties of 1 million or more population that did not qualify as large central metro counties.
- **Medium metro**—Counties of populations of 250,000 to 999,999.
- **Small metro**—Counties of populations less than 250,000.
- **Micropolitan**—Counties in micropolitan statistical areas that have a population of at least 10,000 but less than 50,000.
- **Noncore**—Nonmetropolitan counties that did not qualify as micropolitan.

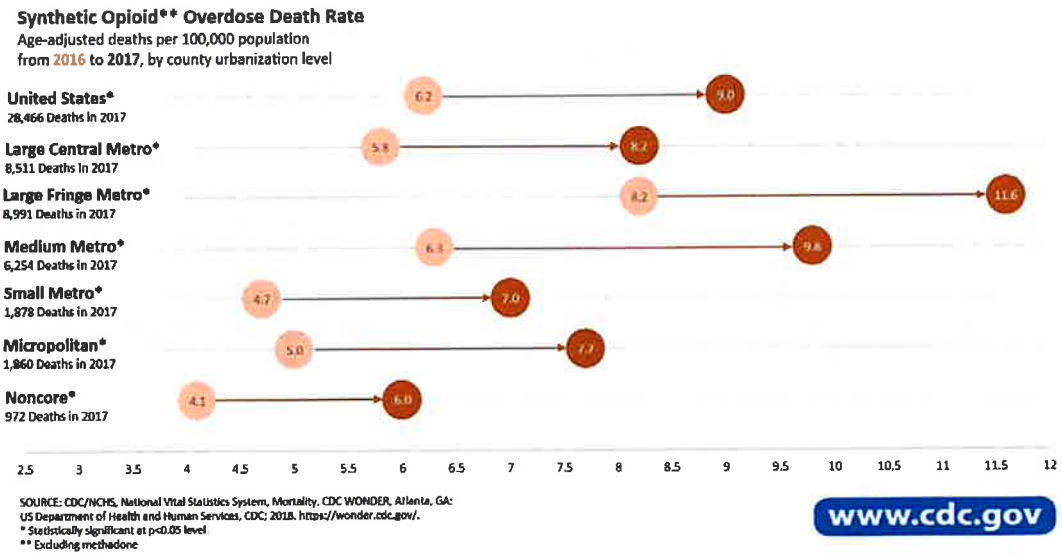
Categories of 2013 NCHS Urban-Rural Classification Scheme for Counties
(https://www.cdc.gov/nchs/data_access/urban_rural.htm)



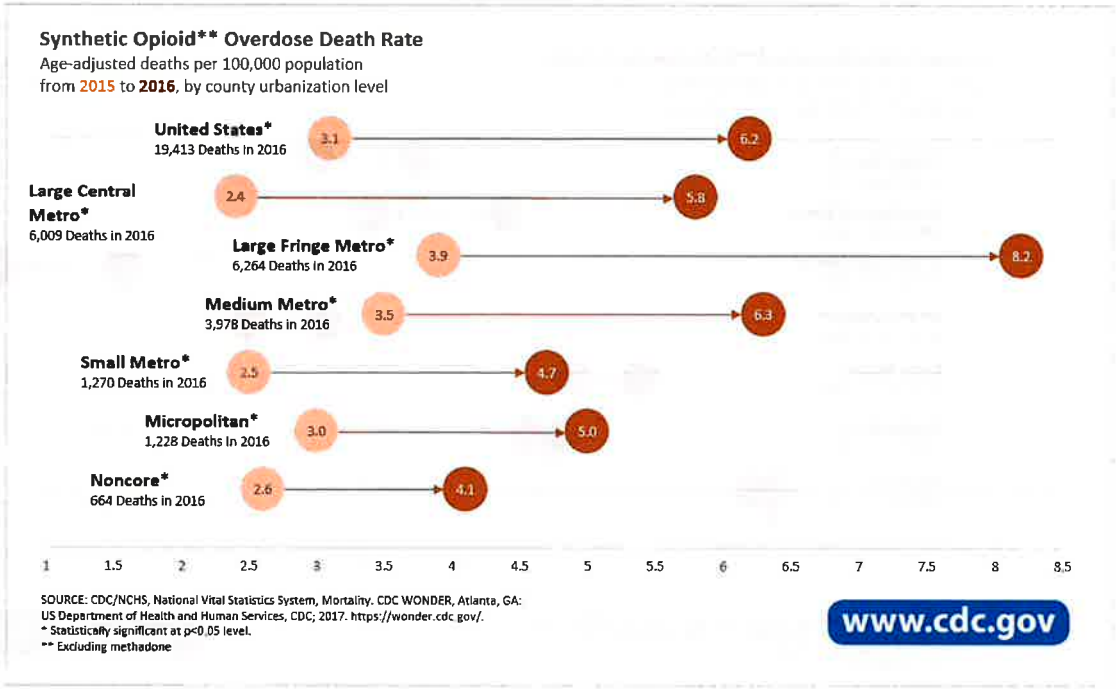
Categories of 2013 NCHS Urban-Rural Classification Scheme for Counties (https://www.cdc.gov/nchs/data_access/urban_rural.htm)

2016-2017 Urbanicity

U.S. Synthetic Opioid Overdose Urbanicity



2015-2016 Urbanicity



Infographics

Fentanyl

- A **synthetic** (man-made) opioid **50x** more potent than heroin and **100x** more potent than morphine.
- **Prescribed** in the form of transdermal patches, tablets, lozenges, or nasal sprays.
- Can also be **illegally** made (**illicitly manufactured fentanyl**) and mixed into other drugs like heroin or cocaine.

Illicitly Manufactured Fentanyl (IMF)

- **Illegally sold** for its heroin-like effect, and linked to recent increases in **overdose deaths**.
- Often pressed into **counterfeit pills** or **mixed** with **heroin** or **cocaine**, with or without the user's knowledge.
- **Fentanyl analogs** are drugs that are **chemically related** to fentanyl and mimic the effects of the drug.

References

1. Wilson N, Kariisa M, Seth P, et al. Drug and Opioid-Involved Overdose Deaths—United States, 2017-2018. MMWR Morb Mortal Wkly Rep 2020;69:290-297.
2. Gladden RM, Martinez P, Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths – 27 states, 2013-2014. Morb Mortal Wkly Rep. 2016;65(33):837-43.
3. Peterson AB, Gladden RM, Delcher C, Spies E, Garcia-Williams A, Wang Y, et al. Increases in fentanyl-related overdose deaths – Florida and Ohio, 2013-2015. Morb Mortal Wkly Rep. 2016;65(33):844-9.

4. O'Donnell JK, Gladden RM, Seth P. Trends in Deaths Involving Heroin and Synthetic Opioids Excluding Methadone, and Law Enforcement Drug Product Reports, by Census Region — United States, 2006–2015. MMWR Morb Mortal Wkly Rep 2017;66:897–903.

5. O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 — 10 States, July–December 2016. MMWR Morb Mortal Wkly Rep 2017;66:1197–1202.

6. O'Donnell J, Gladden RM, Mattson CL, Kariisa M. Notes from the Field: Overdose Deaths with Carfentanil and Other Fentanyl Analogs Detected – 10 States, July 2016-June 2017. MMWR Morb Mortal Wkly Rep. July 2018. 67(27);767–768.

Page last reviewed: March 19, 2020


UNCLASSIFIED
U.S. Department of Justice
Drug Enforcement Administration
2017
NATIONAL
DRUG
THREAT
ASSESSMENT
OCTOBER 2017
DEA-DCT-DIR-040-17
UNCLASSIFIED

FENTANYL AND OTHER SYNTHETIC OPIOIDS

Overview

Fentanyl is a Schedule II synthetic opioid approved for use as a painkiller and anesthetic. The drug's extremely strong opioid properties—both analgesic and euphoric—have made it an attractive drug of abuse for opioid users. Pharmaceutical fentanyl is diverted from healthcare facilities, although usually on a small scale and for personal use or street sales. Fentanyl is also illicitly manufactured in laboratories in China, and likely Mexico, before being smuggled into the United States and distributed in opioid markets. There is little to no evidence that pharmaceutical fentanyl is diverted from these countries, as all fentanyl seizures in the United States have been in powder form, smuggled from China and Mexico, indicating illicitly-produced fentanyl. The relatively small-scale quantities of licit fentanyl being diverted compared to kilogram seizures of illicitly-produced fentanyl, indicates illicitly-produced fentanyl is responsible for the current fentanyl epidemic in the United States.

Availability

Fentanyl is now widely available throughout the United States, with all DEA FDs reporting accessibility to it. Fentanyl is available in both its legitimate and illicit forms. Legitimate fentanyl, also known as pharmaceutical fentanyl, is prescribed by a physician in a variety of forms to include transdermal patches and lozenges. Fentanyl in these forms is diverted from the legitimate market, although on a smaller scale compared to illicitly produced fentanyl. Illicitly produced fentanyl is produced in clandestine laboratories and typically distributed in a white powder form, to be mixed into heroin or pressed into counterfeit opioid prescription pills.

Fentanyl-related substances are also increasingly becoming available throughout the United States. Fentanyl- related substances are substances in the fentanyl chemical family, with similar pharmacological effects, but with minor variations in the chemical structure.

U-4770

The rise of fentanyl paved the way for other synthetic opioids to enter illicit drug markets. In 2016, DEA first encountered U-47700, a synthetic opioid responsible for at least 80 deaths in the United States for the year. It is approximately 7.5 times the potency of morphine, and is abused for its strong opioid properties. U-47700 primarily arrives in the mail from China, and has been seized in powder and tablet form. DEA temporarily placed U-47700 into Schedule I of the CSA in October 2016 upon the finding U-47700 posed an imminent hazard to public safety.

Officer Safety and Fentanyl

Fentanyl is an extremely deadly substance with the European Monitoring Centre for Drugs and Drug Addiction reporting a lethal dose is only 2 milligrams. Only properly trained and outfitted law enforcement professionals should handle any substance suspected to contain fentanyl or a fentanyl-related substance. If you suspect the presence of fentanyl or a fentanyl-related compound, do not take samples or attempt presumptive color testing and follow approved transportation procedures to transport it to the nearest laboratory. For further guidance on safe handling of suspected fentanyl, please see the November 2016 published guidance on CDC's website from the National Institute for Occupational Safety and Health, and the June 2017 DEA publication titled Fentanyl: A Briefing Guide for First Responders, available on DEA's website.

Figure 46. Fentanyl seized from pickup truck.

Source: Bartow County Police Department

Largest Fentanyl Seizure Occurs in Georgia

The largest recorded single seizure of fentanyl to date occurred in March 2016, on I-75 in Bartow County, Georgia. The Bartow-Cartersville Drug Task Force discovered 40 kilograms of fentanyl powder secreted in various hidden compartments on a pickup truck during a traffic stop (see Figure 46).

These substances are typically sourced as a substitute for fentanyl as traffickers attempt to use fentanyl-like substances that are not yet controlled. In most cases, information such as potency and lethal dosage are unknown.

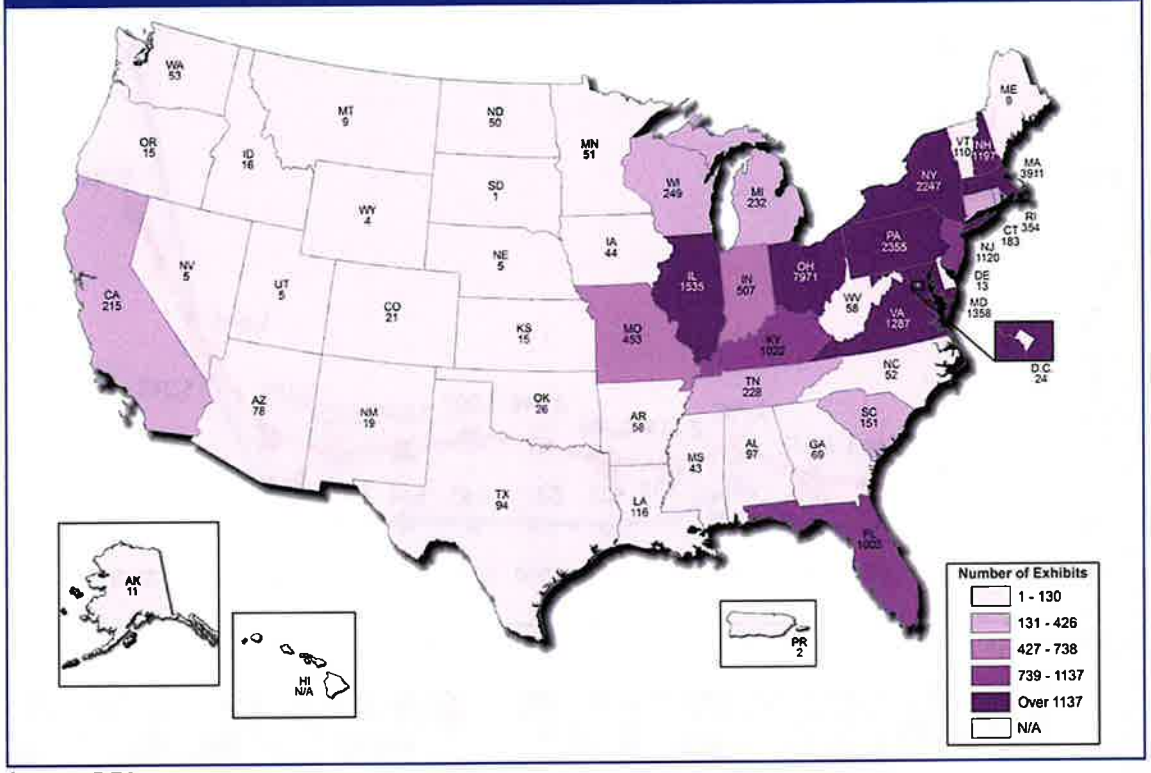
In CY 2016, law enforcement agencies across the United States seized a record-high 287 kilograms of fentanyl; a 72 percent increase from the 167 kilograms seized in 2015. Fentanyl exhibits tested by forensic laboratories and reported to NFLIS in Calendar Year (CY) 2016 shows the large footprint of fentanyl. The data shows a heavy concentration of exhibits in the Northeast, where there has been a historical white powder heroin and opioid problem. Ohio had the greatest number of fentanyl reports, 7,971, in 2016. Massachusetts had the second greatest with 3,911 reports, and Pennsylvania had the third greatest at 2,355 reports (see Figure 47).

Use

Fentanyl and its related compounds are used for their strong opioid properties. Fentanyl is approximately 50 to 100 times more potent than morphine. Like other opioids, fentanyl provides a euphoric high and is incredibly addictive. Adverse effects of fentanyl abuse include nausea, fainting, respiratory failure, and death.

The CDC reported a 79 percent increase in synthetic opioid deaths, from 5,343 in 2014 to 9,580 in 2015. While the synthetic opioid category does include other substances such as Tramadol®, fentanyl largely dominates the category. Additionally, there is a strong relationship between the number of synthetic opioid deaths and the number of fentanyl

Figure 47. Number of Fentanyl Exhibits by State for CY 2016.



Source: DEA

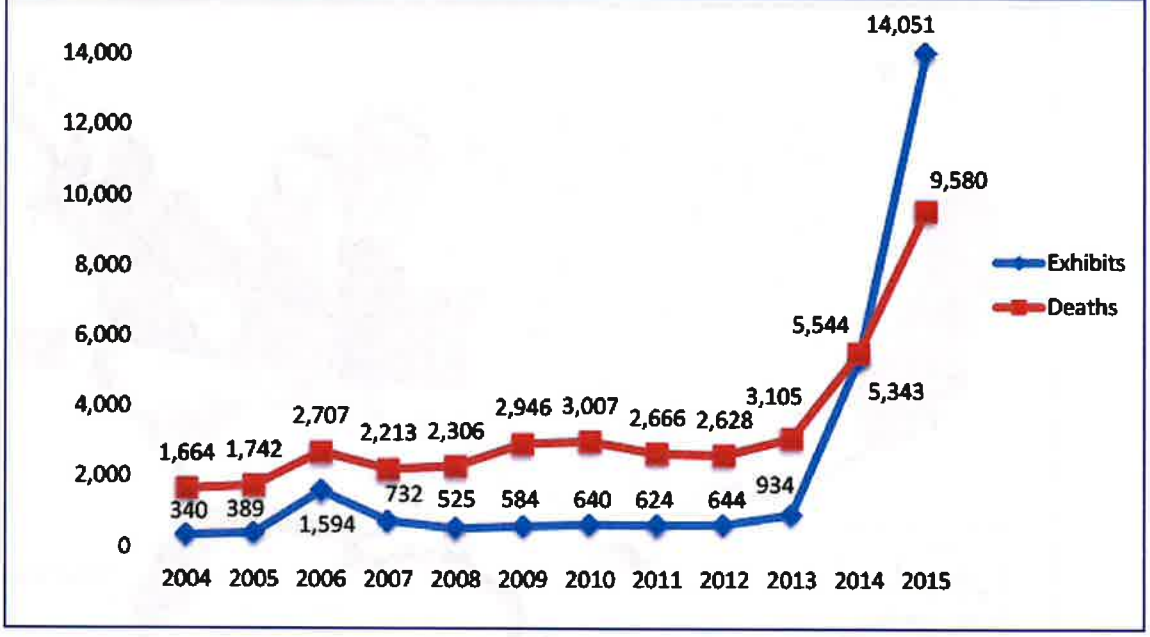
exhibits encountered by forensic laboratories (see Figure 48). When the number of fentanyl exhibits in NFLIS increase, so too does the number of synthetic opioid deaths recorded by the CDC.

Pharmaceutical fentanyl is diverted from healthcare facilities, although the threat posed by diverted fentanyl is smaller than the illicit fentanyl threat. The CDC reports most cases of fentanyl-related morbidity and mortality are linked to illicitly produced fentanyl. Pharmaceutical fentanyl is usually diverted by insiders with access to the drug and stolen to satisfy a personal addiction, or for street-level sales. Users can extract the fentanyl from the gel matrix in transdermal patches (see Figure 49) to smoke or ingest the fentanyl, and intravenous fentanyl solution can be injected directly into the bloodstream.

Illicitly-produced fentanyl is the main type of fentanyl abused in the United States, and is primarily responsible for the fentanyl epidemic. At the outset of the current crisis, illicit fentanyl originally entered illicit drug markets through heroin; fentanyl in powder form is used as an adulterant and mixed into heroin, oftentimes without heroin users knowing. It is increasingly more common for fentanyl to be mixed with adulterants and diluents and sold as heroin, with no heroin present in the product (see Figure 50). In 2016, an overwhelming majority of fentanyl exhibits in NFLIS were fentanyl alone, without heroin, at 22,278 exhibits (see Figure 51). Fentanyl in these forms looks like heroin, is packaged in the same baggies or wax envelopes as heroin, and displays similar stamps or brands as heroin. While many heroin users have no desire to use fentanyl, some do seek it out because of its potency. This can cause public health warnings to have unintended consequences; notifying the community that a particular heroin stamp is known to contain fentanyl or cause overdoses may cause some users to go in search of it.

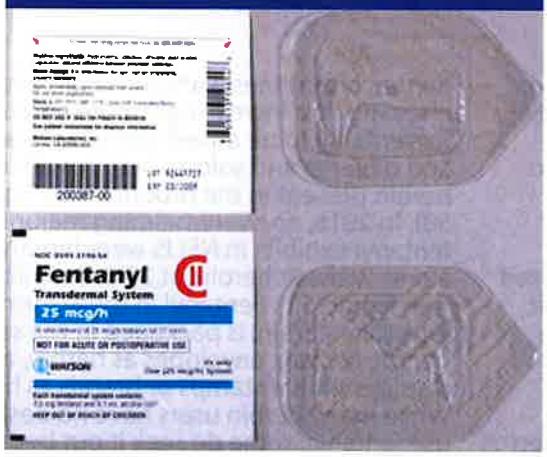
Illicitly-produced fentanyl is increasingly available in the form of counterfeit prescription pills. Fentanyl traffickers use fentanyl powder and pill presses to produce pills that resemble popular prescription opioids, such as oxycodone and hydrocodone (see Figure 52). The pills

Figure 48. Number of Synthetic Opioid Deaths and Fentanyl Exhibits by Year, 2004-2015.



Source: Center for Disease Control and DEA National Forensic Laboratory Information System

Figure 49. Fentanyl Transdermal Patch.



Source: DEA

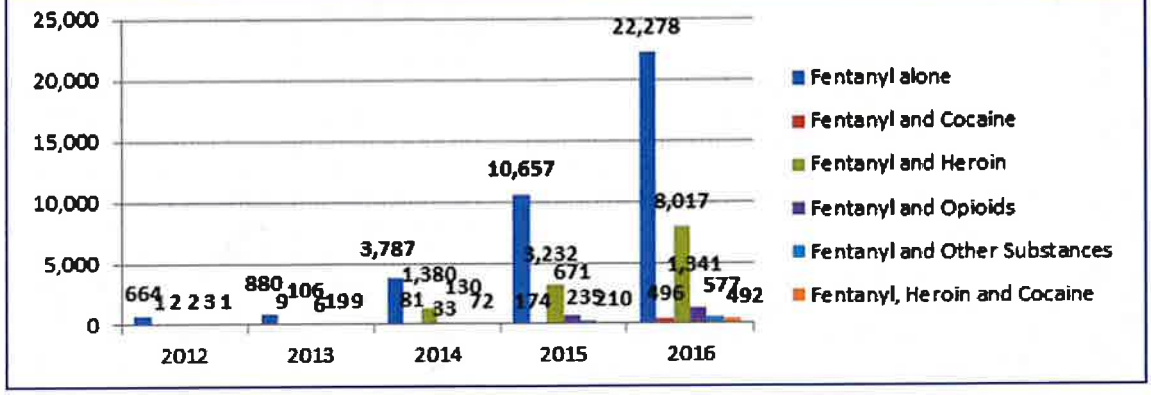
Figure 50. Fentanyl and Heroin Mixture.

Source: DEA

are sold in illicit U.S. drug markets, and users typically do not realize the pills are laced with fentanyl. In many cases, the colorings, markings, and shape of the counterfeit pills were consistent with authentic prescription medications. The presence of fentanyl may only be determined during laboratory analysis.

Expansion of the counterfeit pill market, to include pills containing fentanyl, threatens to circumvent efforts by law enforcement and public health officials to reduce the abuse of opioid medications; the arrival of large amounts of counterfeit prescription drugs containing fentanyl on the market replaces opioid medications taken off of the street. Although a very small percentage of controlled prescription drug users eventually switch to heroin, fentanyl-laced pills give DTOs broader access to the large controlled prescription drug user population, which is reliant upon diversion of legitimate pills. The

Figure 51. Fentanyl Combination Exhibits in NFLIS.



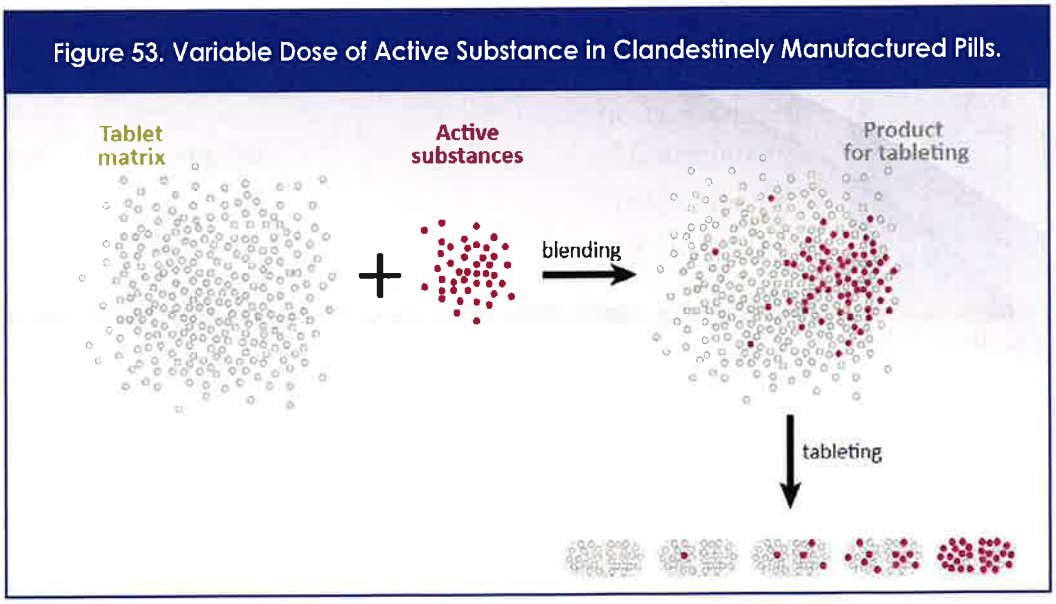
Source: National Forsensic Laboratory Information System August 2017

success traffickers have experienced with secreting fentanyl and related compounds in counterfeit opioid medications will likely result in the emergence of fentanyl and related compounds in a variety of other counterfeit prescription drugs. Between January and March 2016, nine people died from counterfeit Xanax® pills containing fentanyl in Pinellas County, Florida. In March and April 2016, 52 overdoses and 12 deaths occurred in Sacramento, California from counterfeit hydrocodone tablets imprinted with M367. The difficulties in mixing fentanyl into tablet form contribute to such mass overdose events. The amount of fentanyl intended for each tablet is small, and while experienced pill mill

Figure 52. Counterfeit Oxycodone Tablets Containing Fentanyl.

Source: DEA

Figure 53. Variable Dose of Active Substance in Clandestinely Manufactured Pills.



Source: United Nations Office on Drugs and Crime

operators may produce a level of uniformity, amateur operators risk creating hot spots, or areas of higher concentrations of fentanyl in the pills (see Figure 53).

The high profitability of counterfeit prescription pills laced with fentanyl strongly incentivizes traffickers to continue producing them. These pills often retail for between $10 and $20 in illicit street markets, potentially netting traffickers millions of dollars in profit (see Figure 54).

In 2016, law enforcement agencies learned of the availability of fentanyl in new forms, such as on blotter paper, in eye droppers, and in nasal sprays. While the majority of illicit fentanyl is distributed in powder and pill forms, traffickers are experimenting with new preparations to expand the market. New and novel preparations of illicit fentanyl are commonly found on darknet markets.

Production

Illicitly-produced fentanyl, along with its analogues, is manufactured in China and Mexico. Fentanyl is synthesized in laboratories entirely from chemicals, unlike drugs such as heroin, which require plant-based alkaloids. There are two primary methods used to produce fentanyl: the Janssen method and the Siegfried method. The Janssen method is complicated and generally beyond the skill set of novice clandestine laboratory cooks. The Siegfried method was developed in the 1980s, and proves to be much simpler for drug cooks to execute. This method uses the chemical N-phenethyl-4-piperidone (NPP) as its starting point and synthesizes 4-anilino-N-phenethyl- 4-piperidone (ANPP), which is fentanyl's immediate precursor. Since 2015, at least 187 kilograms of ANPP were seized entering the United States at various ports of entry, indicating traffickers are interested in performing fentanyl synthesis either

Figure 54. Potential Fentanyl Profitability.

Drug	Cost Per 1 Kg to DTO	Approximate Number of Kgs Produced from Original Drug Procurement	Wholesale Price per Kg in Massachusetts	Revenue to DTO from 1 Kg
Heroin	$5,000 - 7,000 (Purchased from Colombia)	1 kg	$80,000	$80,000
Pure Fentanyl (99%)	$3,300 -5,000 (Purchased from China)	16-24 kgs	$80,000	$1,280,000 - 1,920,000

Source: DEA

Carfentanil

In 2016, there was an alarming increase in the illicit availability of carfentanil: a fentanyl-related compound 10,000 times more potent than morphine and the most potent commercially used opioid. Carfentanil is a synthetic opioid controlled federally as a Schedule II substance under the Controlled Substances Act and is not approved for use in humans. It is used as a tranquilizing agent by veterinarians in zoos and other large wildlife environments for elephants and other large mammals.

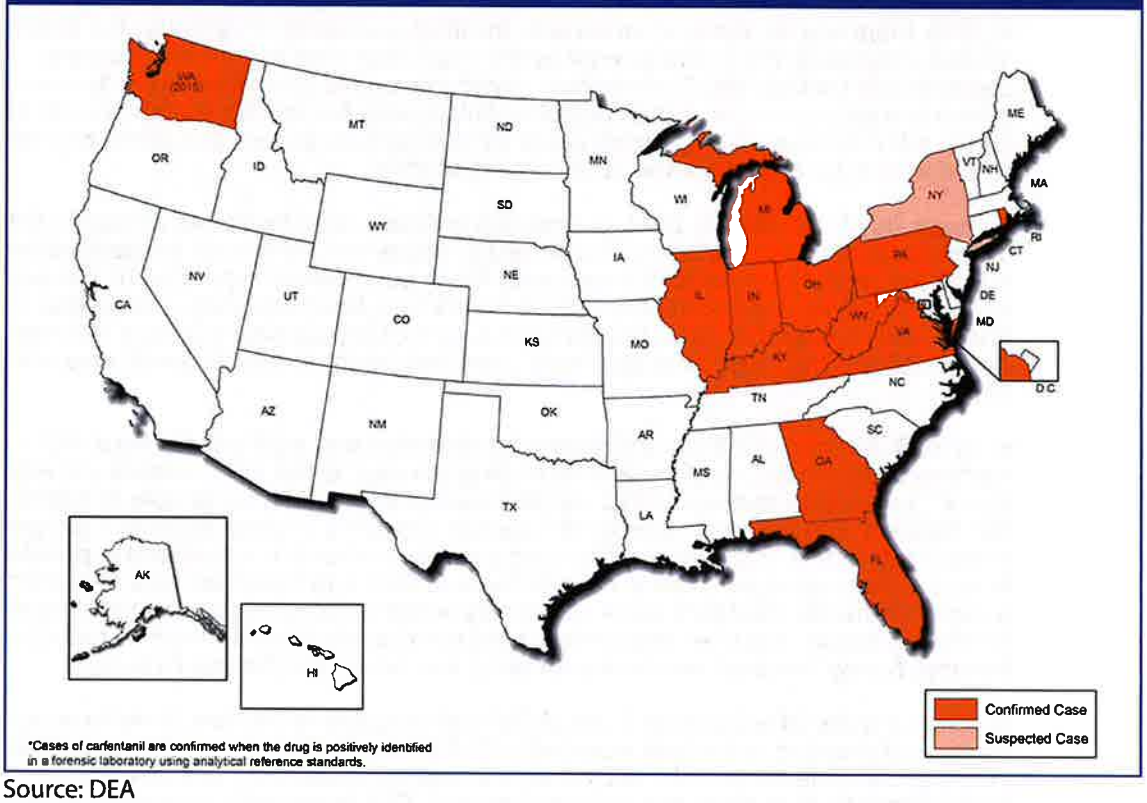
Between July 5 and July 26, 2016, paramedics in Akron, Ohio registered at least 236 drug overdoses with at least 14 being fatal, linked to suspected carfentanil. For perspective, during the January – June 2016 time frame, Akron paramedics responded to 320 overdose incidents. Additional carfentanil overdose events have been reported in Columbus, Ohio. Also, in early September 2016, the Hamilton County, Ohio Coroner's Office confirmed carfentanil was the cause of at least eight overdose deaths in the Cincinnati area since July 2016.

In 2016, DEA's Special Testing and Research Laboratory was notified of at least 413 confirmed identifications of carfentanil in drug samples tested by laboratories in eight states[24]. Laboratory testing in 2015 also revealed a carfentanil drug sample in Washington (see Figure 55). In addition, carfentanil has been identified in blood samples from several overdose deaths in West Virginia. The drug is most commonly encountered in powder form, but it has also been seen in capsule form, tablets, and liquid samples. Carfentanil is most commonly identified either as the only active component or in a mixture with heroin. Carfentanil has been encountered in a number of different mixtures, to include fentanyl; furanyl fentanyl; heroin and fentanyl; and heroin and furanyl fentanyl.

According to the DEA Diversion Control Division's Regulatory Section, there have been no cases of diverted carfentanil reported in DEA's Drug Theft and Loss Database. This indicates the carfentanil in U.S. illicit drug markets is not sourced from DEA registrants, lawful domestic manufacturing, or lawful imports. DEA investigative reporting all indicates the carfentanil that has been seized in multiple states is believed to be arriving from foreign sources via illicit networks and dark web purchases.

[24] Florida, Georgia, Illinois, Indiana, Kentucky, Michigan, Ohio, and Rhode Island.

Figure 55. Confirmed and Suspected Cases of Carfentanil in 2016.



*Cases of carfentanil are confirmed when the drug is positively identified in a forensic laboratory using analytical reference standards.

Source: DEA

Fentanyl Pill Mill Operations

Clandestine fentanyl pill press operations occur in the United States. Traffickers usually purchase powdered fentanyl and fentanyl-related compounds and pill presses from China to create counterfeit pills to supply illicit U.S. drug markets. Under U.S. law, DEA must be notified of the importation of a pill press. However, foreign pill press vendors often mislabel the equipment or send it disassembled to avoid law enforcement detection. In March 2016, the DEA Los Angeles FD executed a federal search warrant at a residential location and seized a counterfeit prescription pill operation using fentanyl and other synthetic opiates. Three pill presses, powder mixing equipment, ventilation equipment, and numerous buckets filled with powder were discovered (see Figure 56).

Figure 56. Pill Presses Used to Manufacture Counterfeit Prescription Pills in Los Angeles.

Source: DEA

domestically or in Mexico. DEA regulates NPP as a List I chemical and ANPP as a Schedule II controlled substance.

Traffickers have become interested in these fentanyl variations because oftentimes they are unscheduled and unregulated, yet still provide similar effects to traditional fentanyl. In 2016, DEA's Special Testing and Research Laboratory found that amongst the category of "fentanyl, fentanyl-related substances, and other new opioids," fentanyl accounted for 68 percent, and fentanyl-related substances and other new opioids accounted for 32 percent.

Transportation and Distribution

Fentanyl is transported into the United States in parcel packages directly from China or from China through Canada, and is also smuggled across the SWB from Mexico. Large volumes of fentanyl are seized at the SWB, although these seizures are typically low in purity – on average approximately 7 percent. Conversely, the smaller volumes seized after arriving in the mail directly from China can have purities over 90 percent and be worth much more than the fentanyl seized at the SWB. In addition to supplying the United States with fentanyl, China is a major supplier of fentanyl and fentanyl-related compounds to Canada and Mexico (See Figure 57). China-sourced fentanyl concealed in mail parcels can be difficult for law enforcement officials to trace back to the original sender due to the use of freight forwarders. The original supplier in China will provide the package to a freight forwarding company or individual, who transfers it to another freight forwarder, who then takes custody and presents the package to customs for export. Additionally, these packages are often incorrectly manifested to avoid law enforcement detection. The combination of a chain of freight forwarders and multiple transferals of custody makes it difficult for law enforcement to track these packages. Fentanyl smuggled across the SWB from Mexico is often concealed in hidden automobile compartments, following traditional drug smuggling techniques.

Fentanyl and fentanyl-related compounds are also sold and distributed through illicit drug markets on the darkweb. Purchasers can use anonymizing internet web browsers to order the substances and have them shipped directly to their homes. These darkweb markets also introduce purchasers to newly available fentanyl-related compounds.

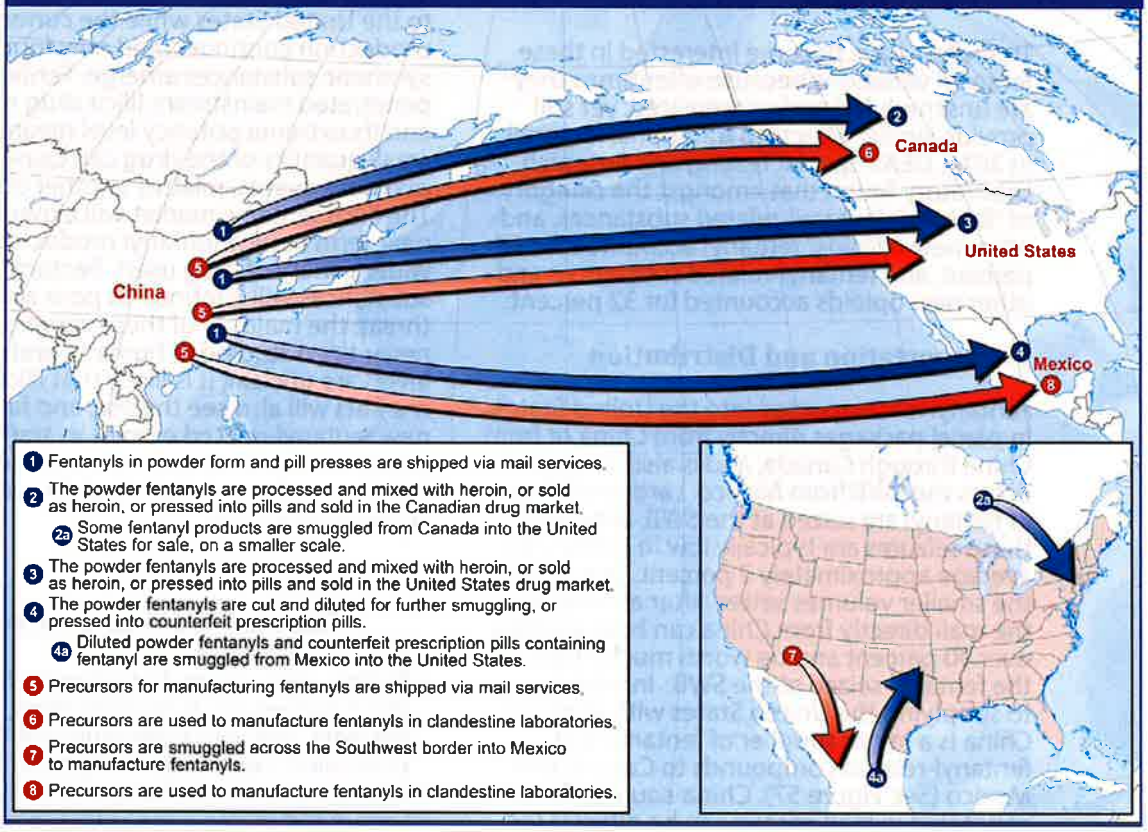
Outlook

Fentanyl will continue to pose a grave threat to the United States while the current illicit production continues, and new forms of synthetic substances emerge. Fentanyl has penetrated mainstream illicit drug markets, and its extreme potency level means a small quantity of the drug can cause mass overdose events, relative to other drugs. The illicit fentanyl market will expand in the near term as new fentanyl products reach a wider variety of drug users. Fentanyl-related substances will continue to pose a serious threat; the majority of these varieties have never been studied in humans, and dosing levels are unclear. It is likely that illicit drug markets will also see the rise, and fall, of new fentanyl-related opioids as traffickers experiment with new compounds to the test the markets, and attempt to evade drug scheduling actions.

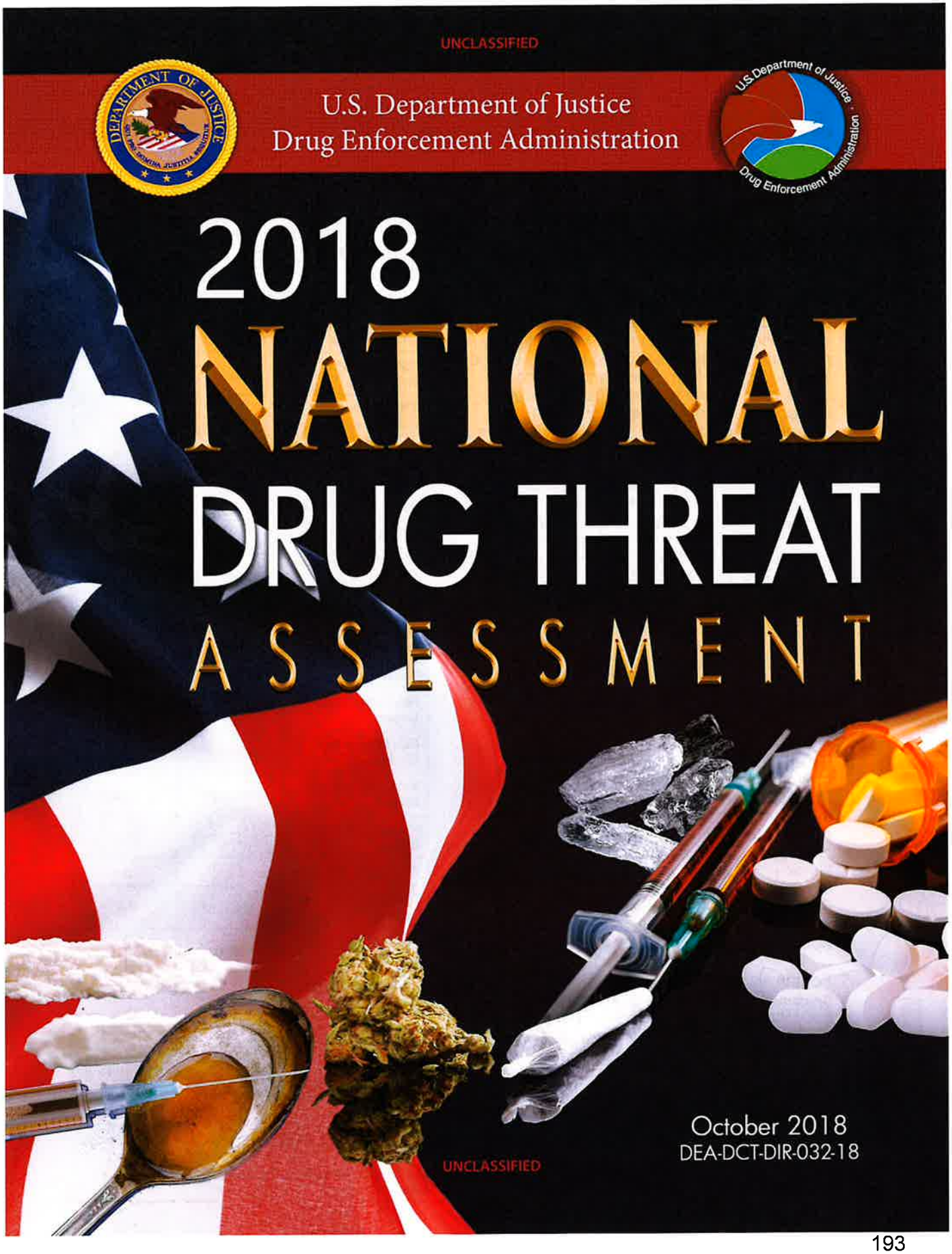
China's Increased Controls

Beijing announced that effective March 2017, carfentanil, furanyl fentanyl, acryl fentanyl, and valeryl fentanyl will be controlled substances in China, in an effort to stem availability of the drugs in the United States. China's October 2015 scheduling of 116 synthetic substances resulted in a decrease of their availability in the United States, and additional scheduling is expected to yield similar results.

Figure 57. Illicit Fentanyl and Fentanyl Precursor Flow Originating in China.



Source: DEA


UNCLASSIFIED
U.S. Department of Justice
Drug Enforcement Administration
2018
NATIONAL
DRUG THREAT
ASSESSMENT
October 2018
DEA-DCT-DIR-032-18
UNCLASSIFIED

FENTANYL AND OTHER SYNTHETIC OPIOIDS

OVERVIEW

Fentanyl is a Schedule II synthetic opioid[20] approved for legitimate use as a painkiller and anesthetic. However, the drug's extremely strong opioid properties make it an attractive drug of abuse for both heroin and prescription opioid users. Clandestinely produced fentanyl is trafficked into the United States primarily from China and Mexico, and is responsible for the ongoing fentanyl epidemic. In contrast, the diversion of pharmaceutical fentanyl in the United States occurs on a small scale, with the diverted fentanyl products being intended for personal use and street sales. Fentanyl continues to be smuggled into the United States primarily in powder or counterfeit pill form, indicating illicitly produced fentanyl as opposed to pharmaceutical fentanyl from the countries of origin. Fentanyl-containing counterfeit pills, along with other new preparations of the drug, demonstrate fentanyl continues to be marketed to new user markets.

AVAILABILITY

Fentanyl is widely available throughout the United States, with all DEA FDs reporting accessibility. Fentanyl is available in both its legitimate and illicit forms. Physicians prescribe legitimate fentanyl in the form of transdermal patches or lozenges. Fentanyl in these forms is diverted from the legitimate market, although on a smaller scale compared to clandestinely produced fentanyl. Illicitly produced fentanyl is synthesized in clandestine laboratories and typically distributed in a white powder form, to be mixed into heroin or pressed into counterfeit opioid prescription pills.

Fentanyl's availability is widespread and increasing, while also becoming more geographically diverse. Eleven out of 21 DEA FDs surveyed indicated fentanyl availability was "High" during the first half of 2017, meaning fentanyl was easily obtained at any time (see Figure 28). The other ten FDs were

Figure 28. DEA Field Division Reporting of Fentanyl Availability in the First Half of 2017 and Comparison to Previous Period.

Field Division	Availability During First Half of 2017	Availability Compared to Second Half of 2016
Atlanta Field Division	Moderate	More
Caribbean Field Division	Low	Stable
Chicago Field Division	High	More
Dallas Field Division	Low	More
Denver Field Division	Low	Stable
Detroit Field Division	High	More
El Paso Field Division	Low	Stable
Houston Field Division	Low	More
Los Angeles Field Division	High	More
Miami Field Division	High	More
New England Field Division	High	More
New Jersey Field Division	Moderate	More
New Orleans Field Division	High	Stable
New York Field Division	Moderate	More
Philadelphia Field Division	High	More
Phoenix Field Division	High	More
San Diego Field Division	Moderate	More
San Francisco Field Division	Moderate	More
Seattle Field Division	High	More
St. Louis Field Division	High	More
Washington Field Division	High	More

Source: DEA Field Division Reporting[21]

[20] In this document, the phrase "synthetic opioid" refers to only those substances which are classified as opioids and have no plant-based material in their production (i.e. fentanyl, fentanyl-related substances, and other novel opioids) and therefore does not include heroin.

[21] Two new DEA Field Divisions, Louisville and Omaha, were opened in 2018, making 23; however, at the time the Field Divisions were surveyed for availability in 2017, there were 21.

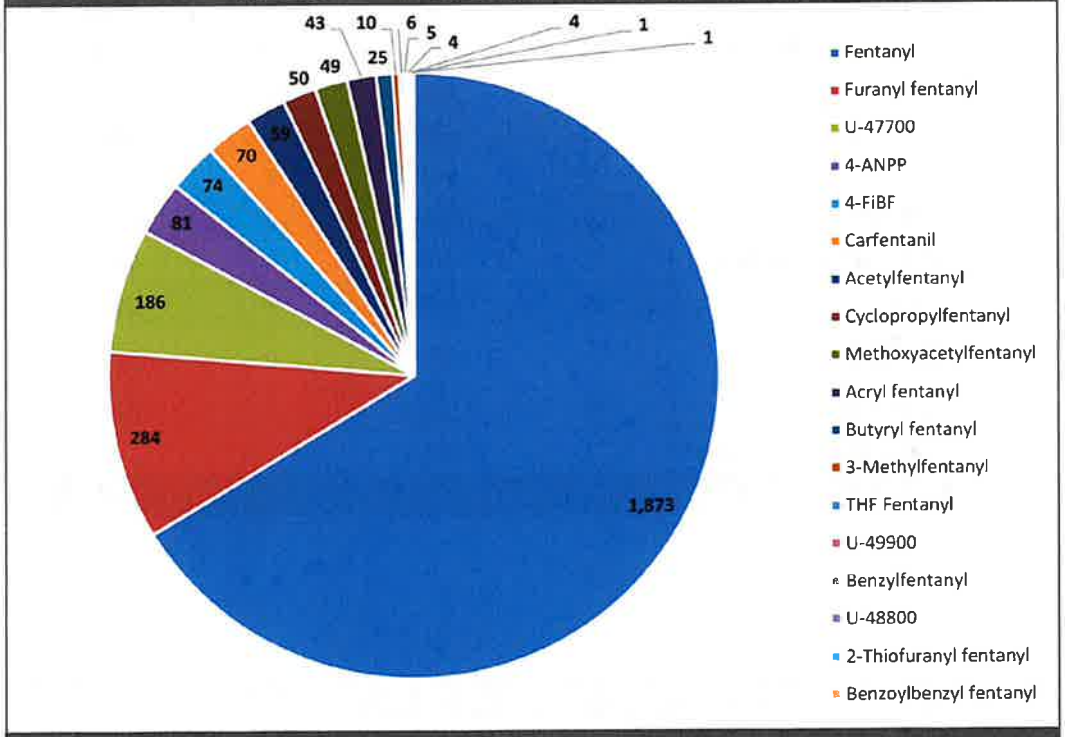
split evenly between reporting fentanyl as having either "moderate" or "low" availability. In addition, 17 out of the 21 FDs indicated fentanyl was "more" available compared to the second half of 2016, demonstrating fentanyl use is increasing across all parts of the United States. The other four FDs indicated fentanyl availability was "stable" compared to the second half of 2016, meaning no FD reported fentanyl availability as "less" in comparison to 2016.

Fentanyl-related substances (FRS) are also increasingly becoming available throughout the United States. These substances are in the fentanyl chemical family, but have minor variations in chemical structure. These substances are typically sold as alternatives to, or substitutes for, fentanyl, but may also be sold as heroin or pressed into counterfeit prescription medications. Most of these substances are not approved for use in humans, so information about potency and lethal dosage are frequently unknown.

Fentanyl continues to be the primary synthetic opioid available in the United States, while more FRS and other new opioids continue to be identified, according to DEA's Emerging Trends Program. In CY 2017, there were 2,825 identifications of fentanyl, FRS, fentanyl precursors, and other new opioids based on exhibits seized and analyzed by DEA. Fentanyl accounted for approximately 66 percent, or 1,873 of the identifications (see Figure 29). Further, of the 1,873 fentanyl identifications, fentanyl was found as the only controlled substance in approximately 43 percent of the identifications and was found in combination with heroin in approximately 47 percent of the identifications. This indicates fentanyl at the retail level is still primarily tied to the opioid market as opposed to the markets for other common controlled substances, such as cocaine or methamphetamine.

The overwhelming majority of fentanyl exhibits analyzed in the United States have been fentanyl in powder form, but fentanyl in counterfeit pill form still represents a significant public health risk and law enforcement challenge in the near term. As of September 2017, DEA had analyzed 583 kilograms of fentanyl powder compared to 17 kilograms of fentanyl in tablet form for CY 2017. However, simply comparing the total weights of each form of fentanyl seized does not provide an accurate representation of the threat posed by fentanyl in counterfeit pills.

Figure 29. Identifications of Fentanyl, Fentanyl Related Substances, Fentanyl Precursors, and Other Synthetic Opioids, CY 2017.



Source: DEA

According to the 2016 NSDUH, there were approximately 3.4 million current misusers of prescription pain relievers compared to 475,000 current heroin users. Traditionally, fentanyl was mixed with or sold as white powder heroin, which potentially limited the overall scope of the fentanyl user market. However, as traffickers have expanded into the sale of fentanyl-containing counterfeit pills, the scope of users who were exposed to fentanyl increased significantly; the prescription pain reliever misuser population is almost ten times that of the heroin user population.

According to national estimates from the National Forensic Laboratory Information System (NFLIS), fentanyl represented approximately the same percentage of all reports of fentanyl and FRS reported between 2015 and 2016. In 2015, fentanyl represented 14,440 reports (84.59%) of the total 17,071 reports of fentanyl and FRS identified in NFLIS. For comparison, in 2016, fentanyl represented 34,204 reports (85.33%) of the total 40,083 reports of fentanyl and FRS identified. This demonstrates that fentanyl continues to be the most popular synthetic opioid available

Figure 30. National Annual Estimates of Fentanyl and Fentanyl-Related Substances Reported in NFLIS, 2015-2016.[22]

Fentanyl and Fentanyl- Related Substances	2015		2016	
	Number	Percent	Number	Percent
Fentanyl	14,440	84.59%	34,204	85.33%
Acetyl fentanyl	2,412	14.13%	1,669	4.16%
Furanyl fentanyl	0	0.00%	2,273	5.67%
Carfentanil	0	0.00%	1,100	2.74%
3-Methylfentanil	1	0.01%	427	1.07%
Butyryl fentanyl	205	1.20%	93	0.23%
Fluoroisobutyryl fentanyl	0	0.00%	82	0.20%
p-Fluoroisobutyryl fentanyl	0	0.00%	76	0.19%
p-Fluorobutyryl fentanyl	2	0.01%	72	0.18%
Valeryl fentanyl	0	0.00%	52	1.13%
Acryl fentanyl	0	0.00%	26	0.06%
p-Fluorofentanyl	8	0.05%	5	0.01%
o-Fluorofentanyl	0	0.00%	3	0.01%
Beta-hydroxythiofentanyl	3	0.02%	0	0.00%
ANPP	0	0.00%	1	0.00%
Acetyl-alpha-methylfentanyl	1	0.01%	0	0.00%
Alpha-methylfentanyl	0	0.00%	1	0.00%
4-Methoxy-butyryl fentanyl[23]	0	0.00%	*	*

Source: DEA National Forensic Laboratory Information System

[22] This table includes drugs submitted to laboratories from January 1, 2015 through December 31, 2016 that were analyzed within three months of the calendar year reporting period.

[23] Estimates that do not meet NFLIS standards of precision and reliability are denoted with "*".

in the United States, even as the total reports of fentanyl and FRS increase each year.

Nevertheless, the number of fentanyl-related substance reports increased significantly between 2015 and 2016, as both more total exhibits of FRS were analyzed and more FRS were analyzed and confirmed for the first time. In 2015, seven FRS contributed to the 2,631 total FRS reports identified in NFLIS. However, in 2016, 12 total FRS combined for 5,879 reports identified, marking a 123 percent increase in total reports in one year (see Figure 30). In 2016, the most commonly identified FRS was furanyl fentanyl, with 2,273 identifications; previously, acetyl fentanyl was the most commonly identified FRS with 2,412 identifications. The most widely available FRS can vary from year to year depending on a combination of user feedback and international control efforts.

According to DEA's Fentanyl Signature Profiling Program[24] (FSPP), in CY 2017, fentanyl seized and analyzed in the United States averaged 5.1 percent pure, based on analysis of approximately 520 fentanyl powder exhibits representing 960 kilograms. FSPP analysis indicated fentanyl available in the United States can range from 0.1 percent to 97.8 percent pure, depending on the source of the fentanyl. DEA and CBP reporting indicate the fentanyl shipped directly from China is typically seized in smaller quantities but with purities commonly testing above 90 percent. By comparison, fentanyl trafficked overland into the United States from Mexico is typically seized in larger, bulk quantities but with much lower purity, with exhibits on average testing at less than ten percent pure.

As fentanyl has become more available in the United States, it has increasingly been seen in new and unique mixtures/cocktails. In 2017, one of the most widely reported and most dangerous of these mixtures was "gray death." This drug cocktail reportedly contained different drugs depending on where in the country it was reported. Across all references to "gray death,"[25] the cocktail is described as a mixture of illicit opioids with the appearance of concrete mix and gray in color. The consistency of the substance described varied, and ranged from a hard and chunky material to a finer powder used for snorting and inhaling smoke. According to the Southeast Florida Fusion Center, "gray death" was comprised of heroin, fentanyl, carfentanil, and U-47700. The "gray death" mixture has been reported in multiple states, to include: Alabama, Indiana, Georgia, Ohio, Pennsylvania, and possibly New York (see Figure 31). In powder form, "gray death" can go airborne, which could be harmful, or even fatal, to law enforcement officers; as such, police are cautioned to avoid field-testing suspected "gray death" and wear appropriate personal protective equipment (PPE).

- Between February 2017 and May 2017, the Georgia Bureau of Investigation had received 50 overdose cases involving "gray death," mostly from the Atlanta area. Samples of reported "gray death" seized from Georgia were a match to a sample submitted from Alabama. However, the amount of each ingredient present differed between the two cases. Additionally, some Georgia samples contained butyrylfentanyl and acrylfentanyl, while others had a completely different composition.
- In May 2017, the Stuart Police Department in Stuart, Florida published an Officer Safety Alert about the possible appearance of "grey death." During that month, officers received reports of a possible overdose in Jensen Beach. Two, possibly three, people took a drug they believed to be "grey death." Two of the subjects suffered overdose effects and were hospitalized. No drugs were recovered.
- In early March 2017, the DEA Buffalo Resident Office (RO) obtained 48 grams of suspected fentanyl, which appeared cement-gray in color (see Figure 32). This gray-colored fentanyl was linked to multiple drug overdose deaths in various states. As such, it is suspected, though unconfirmed, the gray fentanyl may be linked to

[24] DEA's FSPP performs in-depth chemical analyses on fentanyl and fentanyl-related exhibits obtained from seizures made throughout the United States. Analytical methodologies developed by DEA give in-depth reporting on seizures and also link seizures for intelligence purposes. FSPP data is not intended to reflect U.S. market share, but is rather a snapshot of current trends.

[25] The spellings "gray death" and "grey death" are used interchangeably in this report to refer to the same 'brand' of illicit drug cocktail. Reporting from across the law enforcement community contains both spellings.

Figure 31. "Grey Death" in Chunky Rock Form.

Source: Gulf Coast High Intensity Drug Trafficking Area

Figure 32. Gray-Colored Fentanyl Obtained by DEA Buffalo.

Source: DEA

"gray death." The seized fentanyl was powdery in texture as opposed to the chunky texture described by other law enforcement agencies.

Fentanyl available in the United States is often sold under the same or similar "brands" as heroin, which can lead to confusion and wariness among customers depending on what the customer is seeking. For example, one of the most popular "names" associated with high quality heroin is "China White," but distributors across the United States all use "China White" to mean different products. Moreover, it is highly likely many distributors do not know what exactly they are selling when it comes to differentiating between heroin, fentanyl, and fentanyl-laced heroin, as well as differentiating between diverted pills and fentanyl-containing counterfeit pills. This probably means many distributors are not intentionally deceiving customers; instead, suppliers do not always inform distributors specifically what substances or combinations of substances they are selling. Still, other distributors actively cut heroin with fentanyl to extend their heroin supply; however, it is often unclear whether customers in these cases are aware of how/if their heroin has been cut.

- In October 2017, a Boston, Massachusetts-area illicit drug distributor was actively involved in selling heroin and fentanyl in the Boston, Massachusetts and Lynn, Massachusetts areas. This distributor was also reportedly specifically involved in the distribution of kilogram quantities of "China White," described as fentanyl-laced heroin.
- In October 2017, a Phoenix, Arizona-area illicit drug distributor offered to sell pills to multiple customers. Based on the response

DEA EMERGENCY SCHEDULES FENTANYL-RELATED SUBSTANCES

On November 9, 2017, the U.S. Department of Justice (DOJ) announced it was temporarily emergency scheduling all substances chemically related to fentanyl as Schedule I drugs under the Controlled Substances Act (CSA). This order, effective February 2018, signifies criminals who possess, import, distribute, or manufacture any FRS is subject to criminal prosecution in the same manner as for fentanyl and other controlled substances. Overseas chemical manufacturers, aided by illicit domestic distributors, currently attempt to evade regulatory controls by creating structural variants of fentanyl that are not directly listed under the CSA. This action will make it easier for law enforcement officers and federal prosecutors to arrest and prosecute traffickers of all forms of FRS without having to rely on the Analogue Act.

DOJ AND TREASURY DEPARTMENT ANNOUNCE FIRST EVER INDICTMENTS, SANCTIONS AGAINST CHINESE FENTANYL MANUFACTURES

In October 2017, the DOJ announced federal grand juries in the Southern District of Mississippi and the District of North Dakota returned indictments against two Chinese nationals and their North American based traffickers and distributors for separate conspiracies to distribute large quantities of fentanyl and fentanyl analogues and other opiate substances in the United States. The Chinese nationals are the first manufacturers and distributors of fentanyl and other opiate substances to be designated as Consolidated Priority Organization Targets (CPOTs).

Both CPOTs sold/distributed fentanyl and other illegal drugs over the Internet, sometimes operating across multiple websites in order to sell fentanyl and fentanyl analogues directly to customers in the United States. One of the suspects was charged with operating at least two chemical plants capable of producing ton quantities of fentanyl and fentanyl analogues. The suspect monitored legislation and law enforcement activities in the United States and China, modifying the chemical structure of fentanyl analogues produced to evade prosecution in the United States. Another suspect was charged with sending pill presses, stamps, and dies used to shape fentanyl into pills in addition to trafficking in fentanyl and fentanyl analogues. Pill presses were shipped to customers in the United States through the mail or international parcel delivery services.

In April 2018, the U.S. Department of Treasury's Office of Foreign Assets Control (OFAC) identified one of the CPOTs as a Significant Foreign Narcotics Trafficker pursuant to the Kingpin Act. OFAC also designated the CPOT's Hong Kong registered chemical company as being used to facilitate the unlawful importation of fentanyl and other controlled substances into the United States. As a result, any assets in which the CPOT has an interest which are located in the United States or in the possession or control of U.S. persons must be blocked and reported to OFAC. OFAC's regulations generally prohibit all dealings by U.S. persons within (or transiting) the United States that involve any property or interests in property of blocked persons. This represents significant action on behalf of the United States Government to target fentanyl traffickers and chemical companies alleged to have shipped fentanyl from China to the United States.

from one of the customers, the referenced pills were blue fentanyl pills marked with "M 30", made to resemble oxycodone pills. The customer was hesitant when offered the pills and indicated customers are afraid of the pills from Mexico because "they have poison in them." Another customer explained nobody wanted to buy these pills because they had fentanyl, which was killing people, and individuals selling these pills were being charged for the deaths of persons who died from consuming them.

- In July 2017, a Philadelphia, Pennsylvania-area heroin and fentanyl distributor sold what was claimed to be brown/beige colored heroin which was later determined to contain both fentanyl and heroin, according to DEA lab analysis. During this same time period, the distributor discussed being able to obtain "China White," described as high quality fentanyl. Later, in August 2017, the same distributor sold what he/she claimed to be "white" heroin, which was later determined to contain fentanyl and acetyl fentanyl with no heroin.

- In March 2017, a Cincinnati, Ohio-area illicit drug distributor sold heroin, fentanyl, and fentanyl-laced heroin to various customers. The same distributor would often alter the quality of the substance being provided based on the number of customers and how much product the customers were seeking to purchase. Whenever several customers were seeking to purchase one to two ounces of heroin, the distributor would cut the heroin more to stretch supplies. The distributor also sold retail quantities of fentanyl-laced heroin and fentanyl with other cuts.

LARGEST FENTANYL SEIZURE OCCURRED IN QUEENS, NEW YORK APARTMENT

In August 2017, DEA seized 66 kilograms of fentanyl, the largest seizure of fentanyl in United States history (see Figure 33). The shipment was located in an apartment in Queens, New York and was linked to the Sinaloa Cartel. Previously, the largest recorded single seizure of fentanyl was 40 kilograms seized from a pickup truck in Bartow County, Georgia.

Figure 33. Fentanyl Seized from Queens, New York Apartment.

Source: High Intensity Drug Trafficking Area/Domestic Highway Enforcement

USE

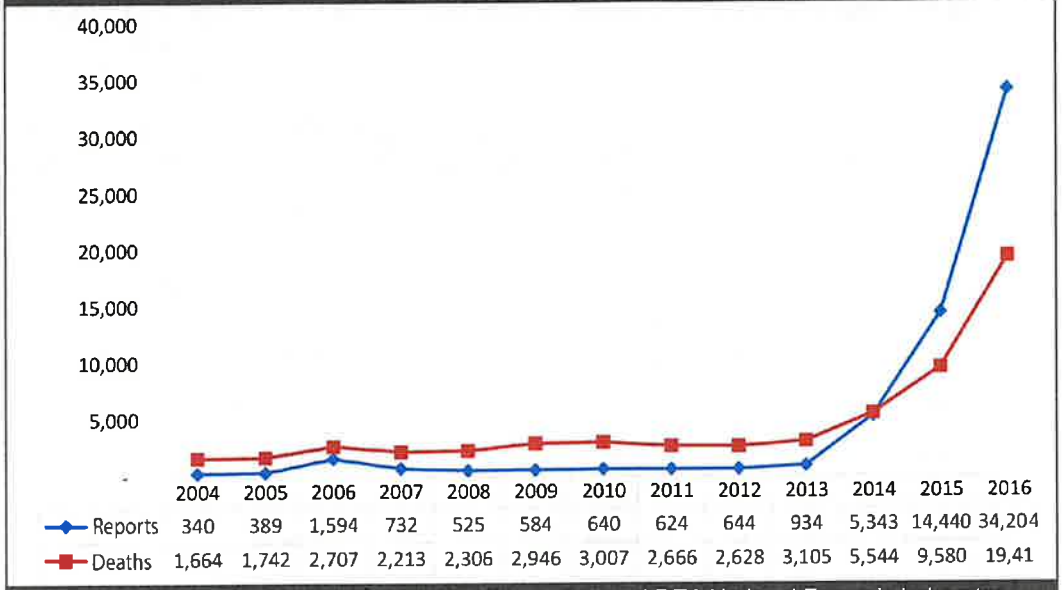
Fentanyl use continues its prevalence in the United States and is a major contributor to the continuing epidemic of drug overdose deaths. Fentanyl's high potency and powerful effects continue to lead to users overdosing and dying in record high numbers. Fentanyl use continues to be most prevalent in areas of the country with high rates of heroin and prescription opioid deaths and availability, indicating fentanyl use still presents the greatest threat among the opioid user population. In addition, the increasing availability and use of fentanyl-containing counterfeit pills demonstrate a relationship with sudden outbreaks of overdose deaths.

The CDC reported a 103 percent increase in synthetic opioid deaths from 2015 to 2016, from 9,580 deaths to 19,413 deaths. Synthetic opioids are now involved in more deaths than any other illicit drug. While the synthetic opioid category does include other substances such as tramadol, fentanyl largely dominates the category. There is a strong relationship between the number of synthetic opioid deaths and the number of fentanyl reports encountered by forensic labs (see Figure 34). When the number of fentanyl reports in NFLIS increase, so too does the number of synthetic opioid deaths recorded by the CDC.

Death certificates continue to report the presence of fentanyl with other substances of abuse, indicating the increased availability of fentanyl. According to highlights from the 2016 mortality data, the annual percentage of fentanyl reported in death certificates reporting heroin, cocaine, psychostimulants, and semi-synthetic opioids has increased significantly since 2014. Moreover, the removal of fentanyl from cocaine-, heroin-, or prescription pain medication-involved overdose data can change the respective trends. The removal of fentanyl-involved deaths from other categories between 2013 and 2016 has these effects: cocaine-involved deaths increased 32 percent versus 110 percent, heroin-involved deaths increased 20 percent versus 87 percent, and semi-synthetic prescription pain medication-involved deaths increased seven percent versus 32 percent.

The increased presence of fentanyl in multiple different drug categories has important public health implications. Tolerances for one class of drugs do not prepare a user for a different class of drugs. As such, individuals who are primarily stimulant users (i.e. cocaine and/or methamphetamine users) are at a significantly increased risk of a fatal overdose if they inadvertently use fentanyl, because of their inexperience with opioids. Additionally, this means messaging directed

Figure 34. Number of Synthetic Opioid[26]-Involved Deaths and Fentanyl Reports in NFLIS by Year, 2004-2016.



	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
Reports	340	389	1,594	732	525	584	640	624	644	934	5,343	14,440	34,204
Deaths	1,664	1,742	2,707	2,213	2,306	2,946	3,007	2,666	2,628	3,105	5,544	9,580	19,41

Source: Centers for Disease Control and Prevention and DEA National Forensic Laboratory Information System

at opioid users (e.g. a warning of a 'bad batch' of heroin) and programs designed to help opioid users (e.g. needle exchanges) may be ineffective at reaching non-opioid users, for whom these treatments and messages are not intended.

The areas of the United States most heavily affected by illicit fentanyl continue to be those parts of the country with high rates of white powder heroin use. In CY 2016, states with the highest rates of synthetic opioid-involved overdose deaths per 100,000 population and the largest number of fentanyl reports contained in NFLIS are correlated with those same metrics for heroin and semi-synthetic prescription pain medications. West Virginia experienced the second highest age-adjusted totals for both heroin- and fentanyl-involved overdose deaths in addition to the highest total of semi-synthetic prescription pain medication-involved overdose deaths per 100,000 population: 14.9 heroin overdoses, 26.3 fentanyl-involved overdose deaths, and 18.5 semi-synthetic prescription pain medication-involved overdose deaths (see Figure 35). Ohio reported the most heroin, fentanyl, and combined hydrocodone and oxycodone reports: 20,964 heroin reports; 9,244 fentanyl reports; 5,702 combined oxycodone and hydrocodone reports (see Figure 36).

Fentanyl's top ten list for overdoses shares three states—Ohio, Connecticut, and Massachusetts— in common with heroin's top ten list for overdoses, and shares two states—Rhode Island and Maine— in common with semi-synthetic prescription pain medications' top ten overdose list (see Figure 37). The top ten lists for NFLIS reports among all three drugs shared three states: Ohio, Pennsylvania, and New York. In addition, NFLIS reports demonstrate a strong link between the top states for heroin and fentanyl reports. These two substances share four states in common on their respective top ten NFLIS reports list: Illinois, Massachusetts, Maryland, and Virginia (see Figure 38). In comparison, only one state—Florida—was linked between fentanyl and semi-synthetic prescription pain medication lab reports, possibly because of Florida's history as a state with high levels of prescription drug abuse.

It is increasingly more common for fentanyl to be mixed with adulterants and diluents and sold as heroin, with no heroin present in the

[26] In 2014, 76 percent of all synthetic opioid-involved deaths specifically mentioned fentanyl.

Figure 35. Top Ten States by Age-Adjusted Rate of Drug-Involved Overdose Deaths Each for Heroin, Fentanyl, and Semi-Synthetic Prescription Pain Medications, CY 2016.

Heroin		Fentanyl		Semi-Synthetic Prescription Pain Medication	
States	Death Rate	States	Death Rate	States	Death Rate
District of Columbia	17.3	New Hampshire	30.3	West Virginia	18.5
West Virginia	14.9	West Virginia	26.3	Utah	11.5
Ohio	13.5	Massachusetts	23.5	Maine	10.8
Connecticut	13.1	Ohio	21.1	Maryland	10.7
Maryland	10.7	District of Columbia	19.2	Tennessee	10.2
New Jersey	9.7	Maryland	17.8	Kentucky	9.3
Massachusetts	9.5	Rhode Island	17.8	Rhode Island	8.1
Vermont	8.7	Maine	17.3	Nevada	7.6
Illinois	8.2	Connecticut	14.8	New Mexico	7.5
New Mexico	8.2	Kentucky	11.5	District of Columbia	7.4

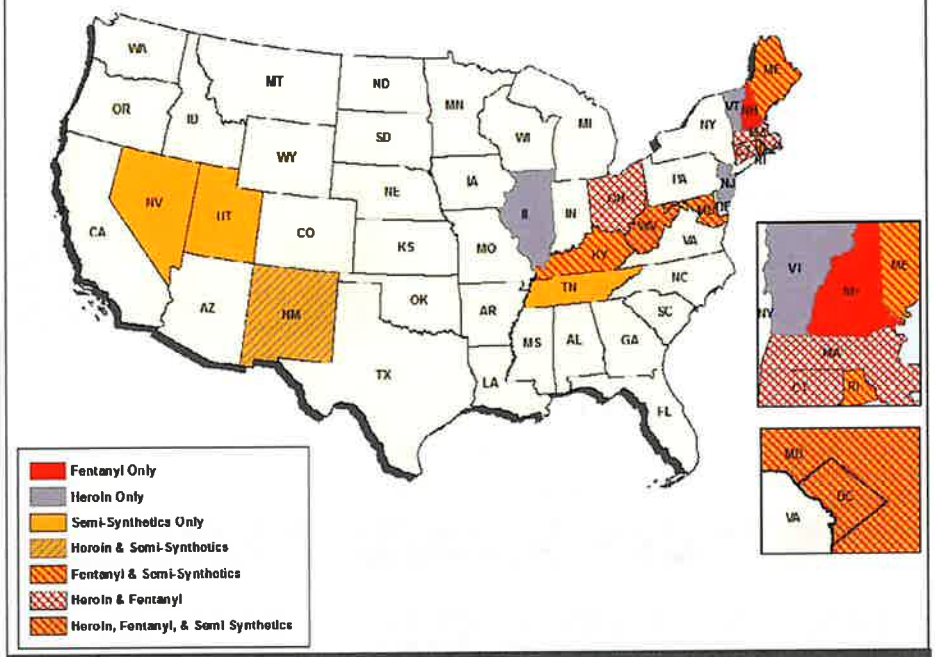
Source: DEA and Centers for Disease Control and Prevention

Figure 36. Top Ten States by Number of NFLIS Reports Each for Heroin, Fentanyl, and Combined Hydrocodone and Oxycodone, CY 2016.

Heroin		Fentanyl		Hydrocodone and Oxycodone	
States	Reports	States	Reports	States	Reports
Ohio	20,964	Ohio	9,224	Ohio	5,702
Pennsylvania	17,222	Massachusetts	6,028	Arkansas	3,533
New Jersey	14,970	Pennsylvania	3,173	Tennessee	3,478
California	12,837	New York	2,365	Virginia	3,331
Illinois	11,240	New Jersey	1,770	Georgia	3,237
New York	10,597	Maryland	1,587	Louisiana	2,709
Massachusetts	9,461	Illinois	1,582	Florida	2,695
Maryland	7,933	New Hampshire	1,524	Kentucky	2,655
Virginia	6,584	Virginia	1,450	Pennsylvania	2,537
Texas	5,212	Florida	1,137	New York	2,403

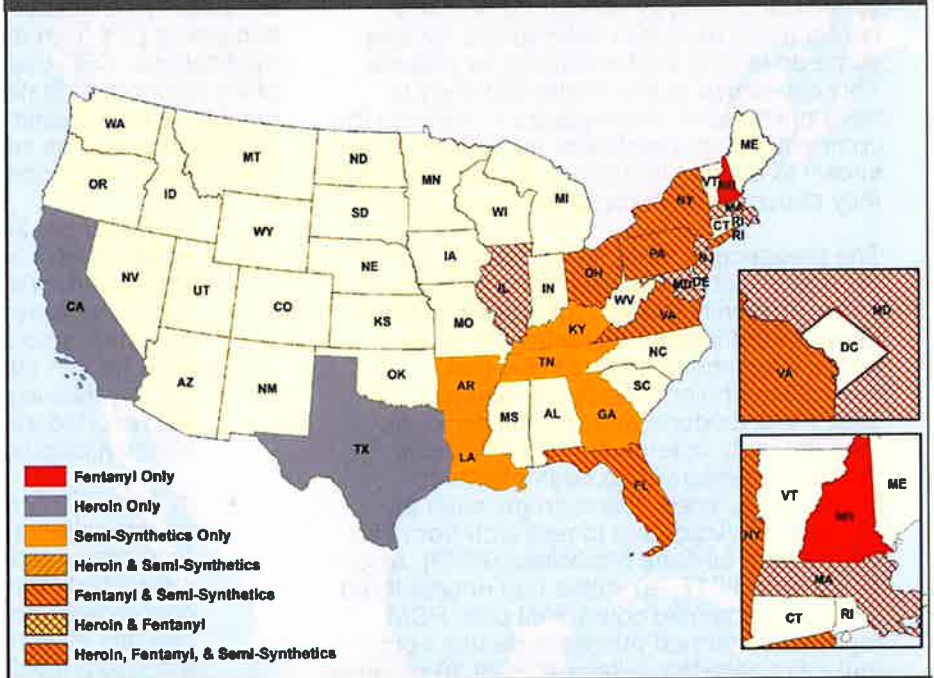
Source: DEA

Figure 37. Top Ten States with Most Drug Poisoning Deaths Per 100,000 Population Each for Heroin, Fentanyl, and Prescription Opioids, CY 2016.



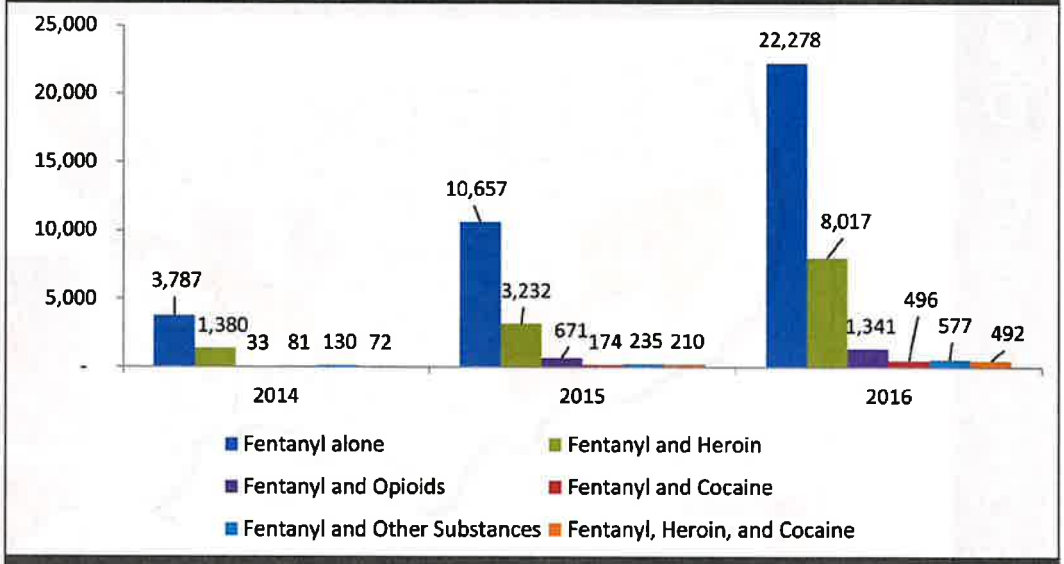
Source: DEA and Centers for Disease Control and Prevention

Figure 38. Top Ten States with Most NFLIS Submissions Each for Heroin, Fentanyl, and Prescription Opioids, CY 2016.



Source: DEA

Figure 39. Fentanyl Combination Reports in NFLIS, 2014 - 2016.



Source: DEA National Forensic Laboratory Information System, August 2017

product. In 2016, an overwhelming majority of fentanyl exhibits in NFLIS were fentanyl alone, without heroin, at 22,278 reports (see Figure 39). DEA reporting reveals fentanyl in these forms possesses the following qualities: looks like heroin, presents in the same packaging as heroin, and displays similar stamps or brands as heroin. While many heroin users have no desire to use fentanyl, some do seek it out because of its potency. This can cause public health warnings to have unintended consequences; notifying the community that a particular heroin stamp is known to contain fentanyl or cause overdoses may cause some users to go in search of it.

The presence of fentanyl-containing counterfeit pills in an area is increasingly associated with spikes in overdose deaths. Fentanyl traffickers use fentanyl powder and pill presses to produce pills that resemble popular prescription opioids such as oxycodone and hydrocodone. As the popularity of fentanyl-containing pills increases, fentanyl has been observed in non-opioid prescription drugs, such as alprazolam. According to research from The Partnership for Safe Medicines (PSM), as of September 2017, 40 states had encountered fentanyl-containing counterfeit pills. PSM reported confirmed overdose deaths from fentanyl-containing pills in at least 16 of those states. The other 24 states probably had deaths attributable to fentanyl-containing pills; however, because awareness of fentanyl-containing pills was limited when research started in 2015, those deaths may not have been investigated for counterfeit drugs. In many cases, the colorings, markings, and shape of the counterfeit CPDs were consistent with authentic prescription medications, meaning users would not necessarily be able to identify fentanyl-containing pills from authentic prescription medications. CPD users may be unaware of the strength of fentanyl-containing pills compared to authentic diverted prescription medications and as such are more susceptible to overdosing.

- In November 2017, the Mississippi State Crime Lab found fentanyl in the system of a recently deceased person who overdosed by taking an unknown amount of pills. This death was the fifth overdose in Madison County, Mississippi for 2017. The lab reported seeing an increase in fentanyl disguised as oxycodone.
- In June 2017, more than two dozen patients were admitted to an emergency room in Macon, Georgia over a two-day-span after ingesting counterfeit Percocet pills. The patients all admitted to having taken the pills but did not initially suspect them to be counterfeit. Analysis later revealed the pills contained a

mix of various substances including cyclopropyl fentanyl and U-47700.

- In March 2017, the Medical Examiner's Office in Maricopa County, Arizona reported 32 confirmed overdose deaths from counterfeit pills containing fentanyl between May 2015 and February 2017. The DEA Heroin Enforcement Action Team attributed the fatalities to fentanyl-containing counterfeit oxycodone pills smuggled into the United States by Mexican DTOs. In addition to fentanyl, nearly 75 percent of the overdoses contained dipyrone, a painkiller banned for use in the United States since 1977.

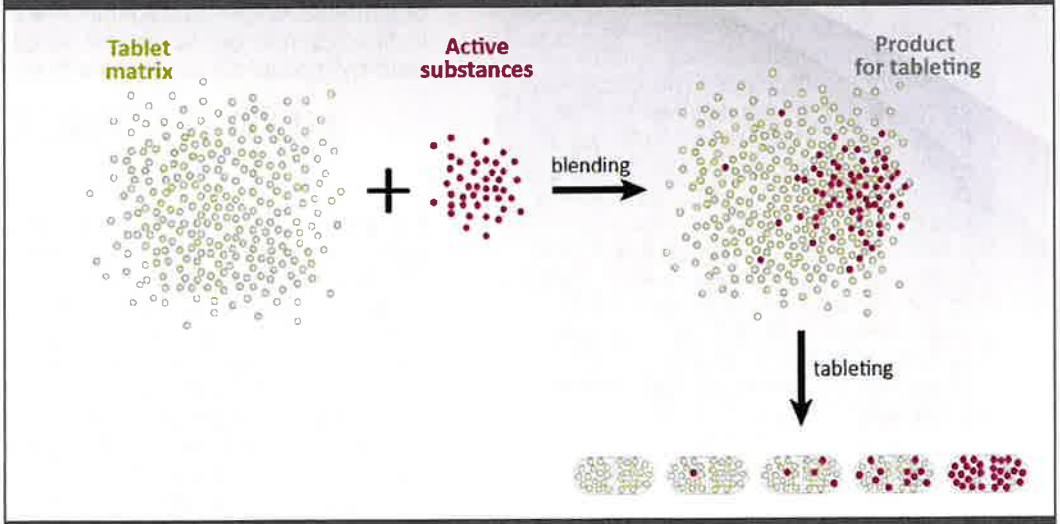
The variable amount of fentanyl present in fentanyl-containing pills is another major contributor to pills' lethality. According to DEA's FSPP, in CY 2017, the average fentanyl-laced tablet contained 1.1 milligrams of fentanyl with a range of 0.03 to 1.99 milligrams per tablet, based on an analysis of 26 tablet exhibits representing nine kilograms. This range of purities represents a large degree of variability in the amount of active substance in each fentanyl-laced pill and/or in each batch of fentanyl-laced pills (see Figure 40). Clandestine pill mill operators create hot spots, or areas of higher concentration, of fentanyl in batches of pills due to improper mixing. This means even fentanyl-containing counterfeit pills from the same batch and appearing simultaneously in a market could be very different in terms of their potential lethality due to variations in milling operations.

PRODUCTION

Illicitly-produced fentanyl and FRS are manufactured in China and Mexico. Fentanyl is synthesized in laboratories entirely from chemicals and requires no plant material to produce, unlike heroin. There are two primary methods to synthesize fentanyl: the Janssen method and the Siegfried method. Clandestinely-produced fentanyl is synthesized using the Siegfried method, as it is simpler for DTO cooks to follow the steps involved. This method can use N-phenethyl-4-piperidone (NPP) as its starting point and synthesizes 4-anilino-N-phenethyl-4-piperidone (ANPP), an immediate precursor to fentanyl. DEA has regulated both NPP and 4-ANPP as these substances have no legitimate purpose other than as precursors to synthesize fentanyl.

In 2018, China's Ministry of Public Security announced scheduling controls on both NPP and 4-ANPP; the controls took effect February 1, 2018. In total, China has domestically controlled 138 NPS, to include

Figure 40. Variable Dose of Active Substance in Clandestinely Manufactured Pills.



Source: United Nations Office on Drugs and Crime

23 synthetic opioids. Notable synthetic opioids controlled by China include, but are not limited to, carfentanil, furanyl fentanyl, valeryl fentanyl, and acryl fentanyl. In October 2017, ANPP and NPP were included in Table I of the Convention against Drugs and Psychotropic Substances of 1988, which placed them under international control. These new restrictions will likely make synthesizing fentanyl more difficult in the near term for DTOs currently reliant on receiving already synthesized NPP. However, DTOs with trained chemists will likely be able to either synthesize NPP or else switch to another method of fentanyl synthesis. DTOs have consistently demonstrated the ability to adapt to precursor chemical restrictions, such as with methamphetamine, all while maintaining a consistent supply of product to the United States.

FENTANYL PRODUCTION LABORATORY SEIZED IN MEXICO FOR THE FIRST TIME SINCE 2016

In November 2017, a Mexican Army patrol deployed to a remote part of Sinaloa state discovered what was later confirmed as a fentanyl production laboratory, the first such discovery in Mexico since 2006. Mexican authorities seized 809 grams of NPP; 1,442 grams of ANPP; 80 liters and 789 grams of noscapine; and 66 grams of fentanyl at the site, in addition to laboratory equipment. The discovery suggests lab operators were using the Siegfried method to synthesize fentanyl at this location, supporting previous United States Government (USG) assessments that Mexico was likely a source, alongside China, for illicitly-produced fentanyl in the United States. Neither NPP nor ANPP have any legitimate uses outside of being precursors used to synthesize fentanyl, according to DEA laboratory information.

TRANSPORTATION AND DISTRIBUTION

Fentanyl is transported into the United States in parcel packages directly from China or from China through Canada, and is also smuggled across the SWB from Mexico. Large volumes of fentanyl are seized at the SWB, although these seizures are typically low in purity, less than ten percent on average. Conversely, the smaller volumes seized after arriving in the mail directly from China can have purities over 90 percent.

Because of the differences in both seizure size and average purity, it is currently not possible to determine which source, Mexico or China, is the greater direct threat as a supplier of fentanyl to the United States. While seizures likely originating in Mexico represent the largest total gross weight of fentanyl seized in the United States, the overall low purity of this fentanyl means a relatively small portion of a given fentanyl seizure is actually fentanyl. Fentanyl sourced from China arrives in significantly smaller quantities than fentanyl sourced from Mexico, but due to its exceptionally high purity, it both poses a greater risk to the purchaser/user and can be adulterated many more times. DEA reporting also indicates Mexican traffickers order fentanyl from China, adulterate it, and smuggle it into the United States themselves, meaning an unknown amount of seized Mexican parcels containing fentanyl are ultimately of Chinese origin. In addition, Mexican traffickers' primary source of supply for fentanyl precursor chemicals is also China.

MEXICO-SOURCED FENTANYL

Fentanyl trafficked by Mexican TCOs is typically in multi-kilogram quantities and is combined with adulterants in clandestine facilities in Mexico prior to it moving into the SWB region. Mexican TCOs most commonly smuggle the multi-kilogram loads of fentanyl concealed in POVs before trafficking the drugs through SWB POEs. According to CBP and DEA reporting, although fentanyl is often seized as a part of poly drug loads (generally cocaine, heroin, and methamphetamine), fentanyl mixtures with other illicit drugs are very uncommon at the wholesale level. This

indicates the mixing of fentanyl with other illicit drugs is most frequently done inside the United States and is not representative of any definitive Mexican TCO strategy.

Fentanyl seizures[27] at SWB POEs increased by 135 percent— from 223 kilograms to 524 kilograms— between CY 2016 and CY 2017. The CBP San Diego Field Office AOR remains the primary entry region for fentanyl entering the United States via the SWB (see Figure 41). Approximately 85 percent of the fentanyl seized— 447 kilograms of 524 kilograms— entering the United States via the SWB flowed through the San Diego POE in CY 2017. During this timeframe, personally operated vehicles were the conveyance for 74 percent of the fentanyl seized, by weight, at SWB POEs. The second largest volume of flow— 14 percent of all the fentanyl seized along the SWB— was seized in the CBP Tucson Field Office AOR in CY 2017. In comparison, during CY 2016, the CBP San Diego Field Office AOR accounted for 91 percent of all the fentanyl seized along the SWB and the CBP Tucson Field Office AOR accounted for nine percent.

For both the San Diego and Tucson Field Office AORs, the number of fentanyl seizures at the POEs increased between CY 2016 and CY 2017. The San Diego Field Office reported 68 fentanyl seizures— compared to 23 in CY 2016— and the Tucson Field Office reported 31 fentanyl seizures— compared to five in CY 2016. These two offices accounted for 99 of the 109 fentanyl seizures at SWB POEs reported in CY 2017.

DEA investigative reporting indicates, the Sinaloa and CJNG Cartels are likely the primary groups trafficking fentanyl into the United States via the SWB. Most CBP fentanyl seizures occur at POEs in Southern California. These POEs are directly adjacent to areas in Mexico with a strong Sinaloa and CJNG presence and both of these cartels are known to smuggle multi-kilogram drug loads through California POEs. The presence of fentanyl comingled with other poly drug loads typical of Sinaloa and CJNG suggests strong links between these TCOs and fentanyl trafficking into the United States.

Figure 41. Custom Border and Protection Fentanyl Seizures by Southwest Border Corridor in CY 2017, with Percent Change from CY 2016.

Source: DEA

[27] These data include only seizures vetted by CBP's Office of Field Operations.

CHINA-SOURCED FENTANYL

Fentanyl and FRS are also being imported in low weight, high concentration shipments via mail and express consignment from China. These shipments are likely being imported by small criminal networks because of the potential for fentanyl and FRS to generate high revenue without the need for allegiance to a larger DTO or Mexican TCO. According to CBP data, nearly all fentanyl seized from international mail and express consignment operations[28] (ECO) originated in China[29] and averaged less than 700 grams in weight. CBP laboratory analysis of similar seizures indicated international mail and ECO seizures are typically over 50 percent pure.

Fentanyl sourced from China accounted for 97 percent of fentanyl seized from the international mail and ECO environments in both CY 2017 and CY 2016. China-sourced fentanyl, by weight, accounted for 165 kilograms of the total 171 kilograms seized from the international mail and ECO environment during CY 2017. This represents a 140 percent increase in the amount of fentanyl sourced from China seized in the mail and ECO environments between CY 2016 and CY 2017— from 69 kilograms to 165 kilograms. To help distinguish between the mail/ECO product line of fentanyl and the SWB product line of fentanyl, CBP's Laboratory and Scientific Services Directorate tested 63 fentanyl samples—nearly all of which were mail/

DEA ARRESTS ONE OF THE MOST PROLIFIC DARK WEB FENTANYL DISTRIBUTORS IN THE UNITED STATES

In November 2016, DEA officials executed a search on a residence in Cottonwood Heights, Utah after investigating what was believed to be a fentanyl distribution operation manufacturing counterfeit fentanyl pills and other counterfeit medications. The search led to the seizure of $1.2 million United States Currency (USC); $2 million virtual currency (VC); 750 grams of fentanyl powder; 400 grams of alprazolam; approximately 200,000 counterfeit oxycodone pills containing fentanyl; approximately 100,000 counterfeit alprazolam pills; and four commercial-grade pill presses (see Figures 42 & 43).

The distribution network operated by purchasing fentanyl and pill presses over the dark web from China and subsequently selling counterfeit pills containing fentanyl over the dark web. The sales were conducted over AlphaBay, which at the time was the largest dark web market. During this time, the suspect was widely considered by customers to be the number one seller of fentanyl-containing pills on AlphaBay due to overwhelmingly positive customer feedback and the ability to ship drugs in bulk quantities. Customers would purchase fentanyl and other counterfeit pills using Bitcoin. The suspect used a close network of friends and associates in and around Salt Lake City to package and mail thousands of orders for customers across all 50 states.

Figure 42. Counterfeit Pills Containing Fentanyl.

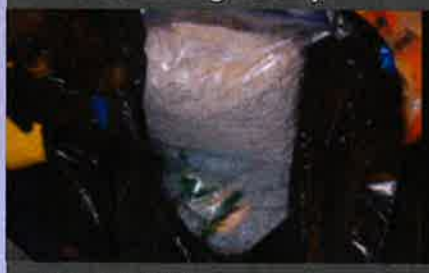


Figure 43. U.S. Currency Found at Suspect's Residence.

Source: DEA

[28] Express consignment operations refer to operations involving parcel courier companies.

[29] Use of the term "China" includes both China and Hong Kong for the purposes of this data set.

ECO seizures— and determined 51 percent of the samples tested between 90 and 100 percent purity. Moreover, 79 percent of the samples analyzed were over 50 percent pure, further distinguishing the two product lines.

Criminal indictments relating to fentanyl smuggling in the mail/ECO environment further suggest individuals involved in U.S.-based fentanyl smuggling act alone or as part of relatively small, independent criminal networks. These networks typically distribute fentanyl locally or sell it to others via the Internet. Further, the increasing use of relatively anonymous "dark web"[30] purchases, paid using money service business (MSB) transfers or virtual currency, facilitates fentanyl trafficking in the mail and ECO environments. For instance, AlphaBay, a dark web marketplace shut down by the Federal Bureau of Investigation (FBI) in July 2017, reportedly had over 200,000 users; 40,000 vendors; 21,000 opioid listings; and 4,100 fentanyl listings. Despite this success, the popularity of fentanyl listings on the dark web indicates it is highly likely dark web fentanyl transactions are extensive and are likely to persist. The National Cyber-Forensics and Training Alliance estimates there are between 100-150 fentanyl vendors currently operating on the dark web. Moreover, as of January 2018, FBI analysis identified approximately 700 fentanyl-related sales listings on the current top six English-language dark web marketplaces.

Clandestine fentanyl pill press operations are becoming increasingly popular in the United States due to the profitability of fentanyl pills and the large potential user market. Traffickers typically purchase already synthesized fentanyl and fentanyl-related compounds in powder form, in addition to pill presses available from China, to create counterfeit pills intended for street sales. Under U.S. law, DEA must be notified when a pill press is imported into the country. However, foreign pill press vendors circumvent this requirement by mislabeling equipment or sending equipment disassembled to avoid detection by port authorities or law enforcement. These laboratories are often found in residential areas and can present challenges for local police departments responding to requests for assistance or executing search warrants.

Figure 44. Pill Press Equipment Seized in Richmond, Texas.

Source: DEA

Figure 45. Fraudulent Oxycodone Tablets Containing Fentanyl Seized in Richmond, Texas.

Source: DEA

[30] The dark web refers to the portion of the Internet that is intentionally hidden and is only accessible through encrypted applications, such as TOR.

Figure 46. Counterfeit Oxycodone Pills Containing Fentanyl and U-47700 Seized in Tucson, Arizona.

Source: Arizona High Intensity Drug Trafficking Area

- In May 2017, the DEA San Antonio and Houston Offices executed a search warrant and seized 35 pounds of fraudulent oxycodone tablets containing suspected fentanyl in Richmond, Texas. Additionally, the search revealed four pill presses, one pound of fentanyl powder, 13 pounds of fraudulent Adderall and Xanax tablets containing methamphetamine, one pound of crystal methamphetamine, and multiple weapons (see Figures 44 & 45).
- In February 2017, an investigation conducted by the Arizona High Intensity Drug Trafficking Area (HIDTA), the FBI, and the Pima County Sheriff's Office resulted in the seizure of 3,150 blue tablets with an "M30" imprint in Tucson, Arizona (see Figure 46). The tablet imprints and color are consistent with pharmaceutically manufactured oxycodone tablets. Tucson Police Department Crime Laboratory analysis of four of the tablets revealed the presence of fentanyl in all the tablets. Three tablets also contained U-47700; lidocaine; suspected noscapine;[31] and suspected meconin.[32]

OUTLOOK

Fentanyl will continue to be a serious threat to the United States while the current illicit production continues and fentanyl availability remains prevalent. Fentanyl's lethality will continue to pose challenges and risks to law enforcement and first responders as well as contribute to increasing numbers of overdose deaths. Moreover, new regulations imposed by the United States, China, and Mexico may decrease fentanyl availability and trafficking in the short term but are unlikely to affect long term change, as traffickers will continue to experiment with new FRS and adjust supplies accordingly. Drug traffickers will continue to be drawn to fentanyl because of the high profits associated with its distribution. Additionally, the use of both the open and dark web to obscure transactions and to distribute fentanyl directly to both users and independent drug trafficking organizations presents challenges for law enforcement and policy makers working to restrict the flow of fentanyl to the United States.

[31] Noscapine is an antitussive (cough suppressing) medication popular in Mexico and commonly identified in samples of heroin sourced to Mexico.

[32] Meconin as a substance is an indicator of heroin.

UNCLASSIFIED

U.S. Department of Justice
Drug Enforcement Administration

2019
DRUG ENFORCEMENT ADMINISTRATION
NATIONAL DRUG THREAT ASSESSMENT

DECEMBER 2019
DEA-DCT-DIR-007-20

U.S. DEPARTMENT OF JUSTICE
DRUG ENFORCEMENT ADMINISTRATION

UNCLASSIFIED

EXECUTIVE SUMMARY

The *2019 National Drug Threat Assessment (NDTA)*[a] is a comprehensive strategic assessment of the threat posed to the United States by domestic and international drug trafficking and the abuse of both licit and illicit drugs. The report combines federal, state, local, and tribal law enforcement reporting; public health data; open source reporting; and intelligence from other government agencies to determine which substances and criminal organizations represent the greatest threat to the United States.

National Drug Threat Assessment Scope and Methodology

The *2019 NDTA* is a comprehensive assessment of the threat posed to the United States by the trafficking and abuse of illicit drugs. The report provides strategic analysis of the domestic drug situation during 2018, based upon the most recent law enforcement, intelligence, and public health data available for the period. It also considers data and information from 2017 and earlier, when appropriate, to provide the most accurate assessment possible to policymakers, law enforcement authorities, and intelligence officials.

In preparation of this report, a full year of data is collected for each drug category by DEA Intelligence Research Specialists. DEA Intelligence Research Specialists considered quantitative data from various sources (seizures, investigations, arrests, drug purity or potency, and drug prices; law enforcement surveys; laboratory analyses; and interagency production and cultivation estimates) and qualitative information (subjective views of individual agencies on drug availability, information on the involvement of organized criminal groups, information on smuggling and transportation trends, and indicators of changes in smuggling and transportation methods).

Illicit drugs, and the transnational and domestic criminal organizations that traffic them, continue to represent significant threats to public health, law enforcement, and national security in the United States. The opioid threat (controlled prescription drugs, synthetic opioids, and heroin) continues at ever-increasing epidemic levels, affecting large portions of the United States. Meanwhile, the stimulant threat (methamphetamine and cocaine) is worsening and becoming more widespread as traffickers continue to sell increasing amounts outside of each drugs' traditional markets. New psychoactive substances (NPS) remain challenging and the domestic marijuana situation is evolving as state-level medical and recreational legalization continues. Drug poisoning deaths are the leading cause of injury death in the United States. In 2017[b], drug poisoning deaths reached their

a. Analyst Note: The information in this report is current as of August 2019.
b. Analyst Note: 2017 overdose-related death statistics is the latest available official data.

highest recorded level and, every year since 2011, have outnumbered deaths by firearms, motor vehicle crashes, suicide, and homicide. In 2017, approximately 192 people died every day from drug poisoning (see Appendix A: Figure A2).

Fentanyl[c] and Other Synthetic Opioids[d]: Fentanyl and other highly potent synthetic opioids—primarily sourced from China and Mexico—continue to be the most lethal category of illicit substances misused in the United States. Fentanyl continues to be sold as counterfeit prescriptions pills as traffickers—wittingly or unwittingly—are increasingly selling fentanyl to users both alone and as an adulterant, leading to rising fentanyl-involved deaths. Fentanyl suppliers will continue to experiment with other new synthetic opioids in an attempt to circumvent new regulations imposed by the United States and China.

Heroin: Heroin-related overdose deaths remain at high levels in the United States, due to continued use and availability, while fentanyl is increasingly prevalent in highly profitable white powder heroin markets. Mexico remains the primary source of heroin available in the United States according to all available sources of intelligence, including law enforcement investigations and scientific data. Further, high-levels of sustained opium poppy cultivation and heroin production in Mexico allow Mexican Transnational Criminal Organizations (TCOs) to continue to supply high-purity, low-cost heroin.

Controlled Prescription Drugs (CPDs): CPDs are still responsible for the most drug-involved overdose deaths and are the second most commonly abused substances in the United States. Traffickers continue to manufacture and distribute counterfeit CPDs often-containing fentanyl and other opioids along with non-opioid illicit drugs in attempts to expand their customer base and increase profits. Overall diversion incidents continue to decline; however, CPDs lost in transit or diverted by medical professionals remains a prevalent threat across the United States.

Methamphetamine: Methamphetamine remains widely available, with traffickers attempting to create new customers by expanding into new, non-traditional methamphetamine markets such as the Northeast, or other user bases with new product forms. Most of the methamphetamine available in the United States is produced in Mexico and smuggled across the Southwest Border (SWB). Domestic production occurs at much lower levels than in Mexico and seizures of domestic methamphetamine laboratories have declined steadily for many years while overall supply has increased.

Cocaine: Cocaine is a resurgent threat in the United States as domestic indicators—such as seizures, availability, and overdose deaths—remain at elevated levels. Cocaine-involved overdose

c. Unless explicitly stated, the term "fentanyl," when used in this report, refers to clandestinely manufactured and illegally distributed fentanyl and not to pharmaceutical or "licit" fentanyl.

d. In this document, the phrase "synthetic opioid" refers to only those substances, which are classified as opioids and have no plant-based material in their production (i.e. fentanyl, fentanyl-related substances, and other novel opioids) and therefore does not include heroin.

deaths continue to exceed established benchmarks, primarily due to the continued spread of fentanyl into the cocaine supply. In addition, coca cultivation and cocaine production in Colombia, the primary source of supply for cocaine in the United States, remain at high levels.

Marijuana: Marijuana remains the most commonly used illicit drug in the United States. The nature of the marijuana threat continues to evolve, as more states vote on referendums and initiatives as well as pass legislation regarding the possession, use, and cultivation of marijuana. Most states that have legalized marijuana have placed no limits on Tetrahydrocannabinol (THC) potency of marijuana or its associated concentrate products. Consequently, THC potency continues to increase, as does demand. Mexico remains the most significant foreign source for marijuana available in the United States, but domestic marijuana production and availability continues to rise. Black market marijuana production by local, national, and transnational criminal trafficking organizations continues to increase, predominantly in states that have legalized marijuana.

New Psychoactive Substances (NPS): The number of NPS varieties continues to increase worldwide, but remains a limited threat in the United States compared to other widely available illicit drugs. China remains the primary source for the synthetic cannabinoids and synthetic cathinones trafficked into the United States. The availability, popularity, and the public health threat of specific NPS varieties in the United States changes every year, as traffickers experiment to circumvent legal restrictions and discover more potent, and therefore popular, substances.

Mexican TCOs: Mexican TCOs remain the greatest criminal drug threat to the United States; no other groups are currently positioned to challenge them. The Sinaloa Cartel maintains the most expansive footprint in the United States, while the Jalisco New Generation Cartel (Cartel Jalisco Nueva Generación or CJNG) has become the second-most dominant domestic presence over the past few years. Although drug-related murders in Mexico continue to reach epidemic proportions, U.S.-based Mexican TCO members still generally refrain from domestic inter-cartel conflicts, resulting in minimal spillover violence in the United States.

Colombian TCOs: Colombian TCOs' control over the production and supply of cocaine to Mexican TCOs allows Colombian TCOs to maintain an indirect influence on U.S. drug markets. Meanwhile, on-going disputes between the Government of Colombia and the remnants of the Revolutionary Armed Forces of Colombia (FARC) and other Armed Criminal Groups continue to, at times, exacerbate the problem of sustained high-levels of illicit coca cultivation in Colombia. Smaller Colombian TCOs still directly supply wholesale quantities of cocaine and heroin to Northeast and East Coast drug markets.

Dominican TCOs: Dominican TCOs dominate the mid-level distribution of cocaine and white powder heroin in major drug markets throughout the Northeast while also engaging in some street-level sales in the region. Dominican TCOs work in collaboration with foreign suppliers to ship cocaine and heroin directly to the United States from Mexico, Colombia, and the Dominican Republic. Family members

and friends of Dominican nationality or American citizens of Dominican descent comprise the majority of Dominican TCOs, insulating them from outside threats.

Asian TCOs: Due to China's currency control restrictions[e], Asian TCOs have taken advantage of the availability of U.S. dollars belonging to Mexican and Colombian TCOs in the United States by acquiring the U.S. dollars in exchange for the payment of Colombian/Mexican pesos in the respective drug source country. TCOs launder drug proceeds through a variety of means, the primary being a hybrid of trade-based money laundering (TBML) and the black market peso exchange (BMPE). Asian TCOs continue to operate indoor marijuana grow houses in states with legal personal-use or medical marijuana laws. Asian TCOs also remain the primary 3,4-Methylenedioxymethamphetamine (MDMA) source of supply in U.S. markets, trafficking MDMA from China or clandestine laboratories in Canada into the United States.

Outside Continental United States (OCONUS) and Tribal Threats: Cocaine is the principal drug threat in the Caribbean followed by marijuana, with Puerto Rico and the U.S. Virgin Islands (USVI) serving as major transshipment points for both drugs. Methamphetamine and marijuana remain the top two drugs of choice in Guam, with cocaine being a rising threat as an alternative to methamphetamine due to changing prices. The drug threat in Indian Country varies by region and is influenced by the illicit drugs available in major cities near the reservations. Methamphetamine and marijuana remain the most widely abused substances in Indian Country.

Illicit Finance: U.S. drug sales continue to account for tens of billions of dollars in illicit proceeds annually. These proceeds change hands multiple times across various levels of the illegal drug market. Bulk cash smuggling seizure amounts remain at lower levels than in previous years, indicating that TCOs may be employing different methods of moving monetary value through the financial system. While traditional methods of laundering money are still the most widely used, the advent of 21st century methods may increase the complexity of anti-money laundering enforcement activities in the future.

Gangs: National and neighborhood-based street gangs and prison gangs remain the dominant distributors of illicit drugs through street-sales in their respective territories throughout the country. Struggle for control of lucrative drug trafficking territories continues to fuel the majority of the street-gang violence facing local communities. Meanwhile, some street gangs are working with rival gangs to increase both gangs' drug revenues, while individual members of assorted street gangs have profited by forming relationships with friends and family associated with Mexican cartels.

e. China currently has a $50,000 annual foreign exchange limit for its citizens.

FENTANYL AND OTHER SYNTHETIC OPIOIDS

Overview

Fentanyl remains the primary driver behind the ongoing opioid crisis, with fentanyl involved in more deaths than any other illicit drug. Fentanyl and other synthetic opioids are widely available throughout the Great Lakes, Midwest, and the Northeast areas of the United States. The two primary sources of the fentanyl are Mexico and China, where drug traffickers produce fentanyl and other synthetic opioids in clandestine operations. Fentanyl is smuggled into the United States across the SWB as well as through international mail and express consignment shipping services, primarily in powder and counterfeit pill form, indicating clandestinely produced fentanyl as opposed to pharmaceutical fentanyl. Increases in fentanyl-containing counterfeit pills and related fentanyl pill pressing operations in addition to other novel preparations demonstrate traffickers' continued efforts to expand the fentanyl user base.

Availability

Fentanyl availability was high and increasing across the majority of the United States in 2018, highlighting the rapid spread of the drug. For Calendar Year (CY) 2018, 15 of 23 Field Divisions (FDs) (see Appendix A: Figure A1) (65 percent) indicated fentanyl availability was "high" and 21 of 23 FDs (91 percent) indicated fentanyl was "more" available compared to 2017 (see Figure 1). The Caribbean, Dallas, Denver, Houston, New Jersey, Omaha, and San Francisco FDs did not rank fentanyl as highly available. This illustrates that, although fentanyl is trafficked across the SWB and is commonly seized in the Southwestern United States, the Midwest, Great Lakes, and Northeast regions maintain the greatest availabilities of fentanyl.

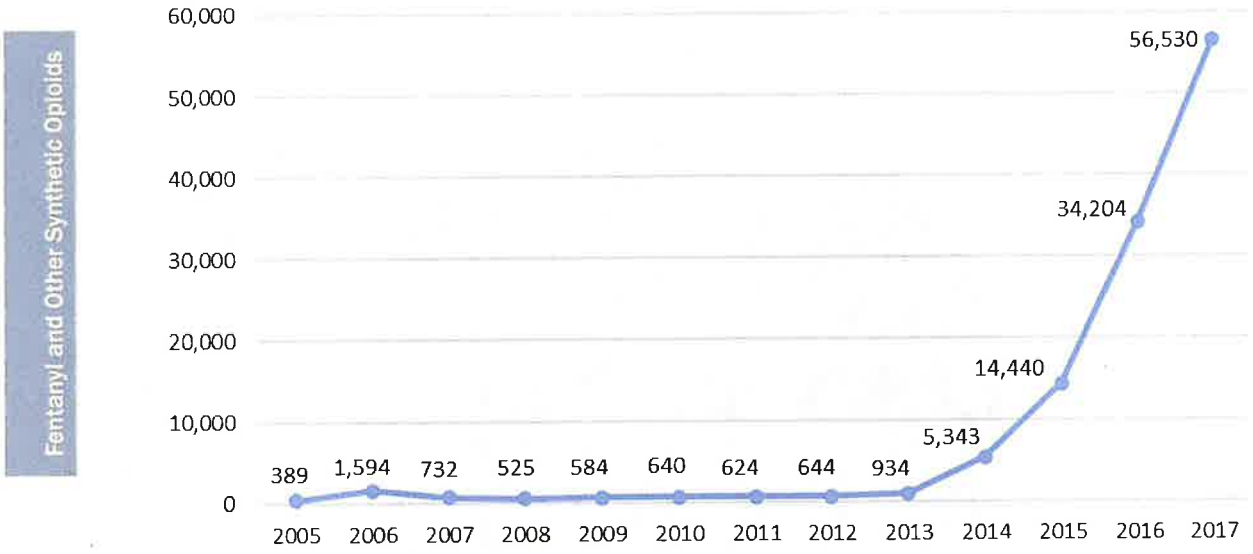
Figure 1. Field Division Reporting of Fentanyl Availability in CY 2018 and Comparison to CY 2017

Field Division	Availability During CY 2018	Availability Compared to CY 2017
Atlanta Field Division	High	More
Caribbean Field Division	Low	More
Chicago Field Division	High	More
Dallas Field Division	Moderate	More
Denver Field Division	Low	More
Detroit Field Division	High	Stable
El Paso Field Division	High	More
Houston Field Division	Moderate	More
Los Angeles Field Division	High	More
Louisville Field Division	High	Stable
Miami Field Division	High	More
New England Field Division	High	More
New Jersey Field Division	Moderate	More
New Orleans Field Division	Stable	More
New York Field Division	High	More
Omaha Field Division	Moderate	More
Philadelphia Field Division	High	More
Phoenix Field Division	High	More
San Diego Field Division	High	More
San Francisco Field Division	Moderate	More
Seattle Field Division	High	More
St. Louis Field Division	High	More
Washington Field Division	High	More

Source: DEA

The total number of fentanyl reports submitted to forensic laboratories continues to increase

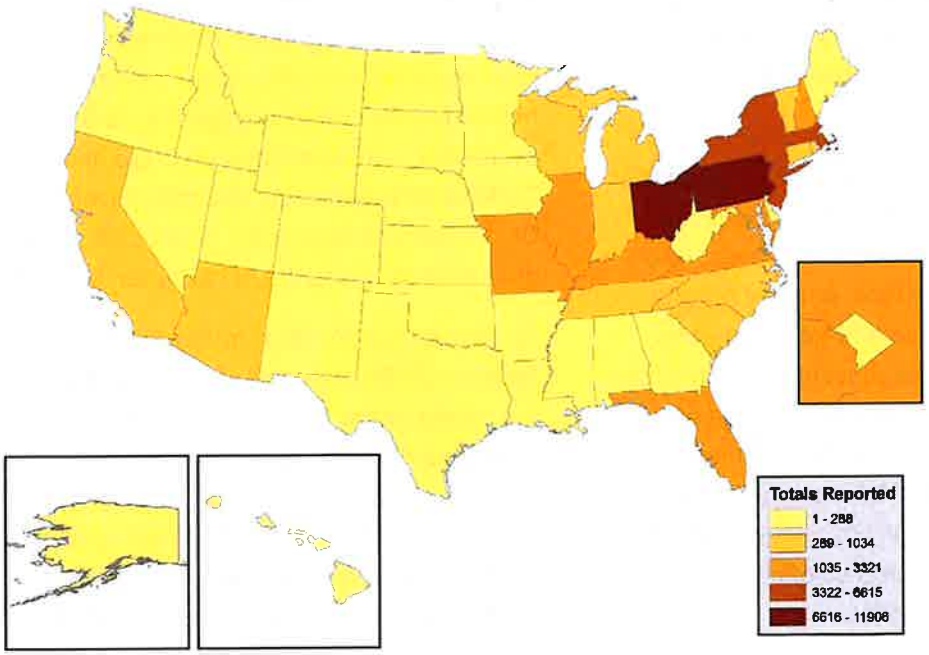
Figure 2. Forensic Laboratory Reports of Fentanyl, 2005 – 2017



Source: DEA

significantly, demonstrating the availability of fentanyl in the United States (see Figure 2). In 2017, there were 56,530 fentanyl reports submitted to the National Forensic Laboratory Information System (NFLIS), which is a 65 percent increase over the 34,204 reports submitted in 2016. Of the top 25 most frequently identified drugs in NFLIS, fentanyl ranked fifth overall and represented 3.57 percent of the top 25 drug reports. For comparison, there were 157,055 reports of heroin, which represented 9.93 percent of the top 25 drug reports. Therefore, while fentanyl availability continues to increase, heroin maintains a significant presence in the U.S. drug market.

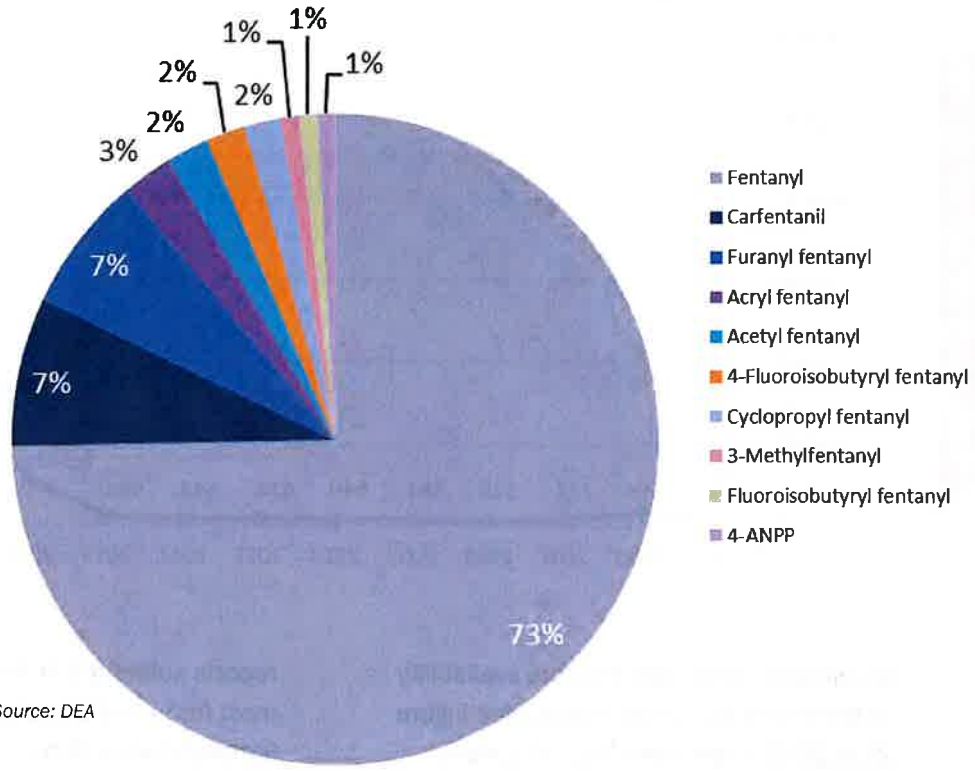
Figure 3. State-level Fentanyl Reports, 2017



Source: DEA

State-level reports in NFLIS continue to show fentanyl's dominant presence in the Great Lakes and Northeast regions of the United States with a lessor presence in the Western United States. Ohio, Pennsylvania, Massachusetts, New

Figure 4. Nationwide Reports of Fentanyl, Synthetic Opioids, and Precursor Chemicals, 2017



Source: DEA

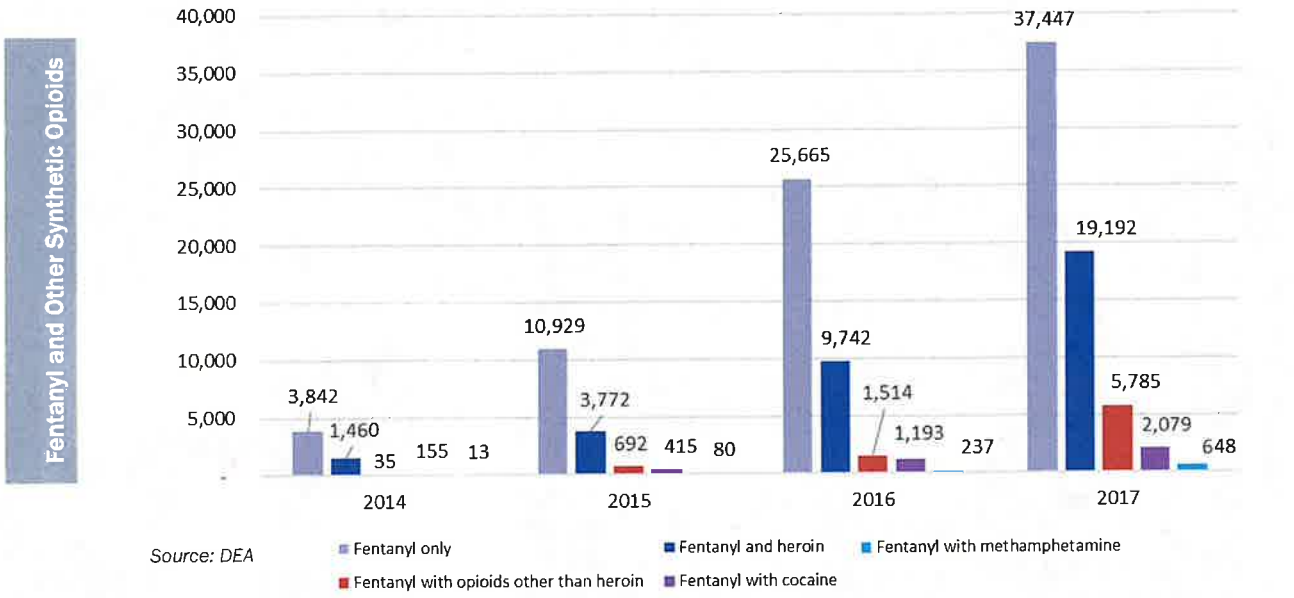
York, and New Jersey had the most fentanyl reports in NFLIS in 2017 (see Figure 3). Moreover, Ohio, Pennsylvania, and New Jersey were among the five states with the most heroin reports in NFLIS in 2017. This further emphasizes the continued overlap between the heroin market and the fentanyl market.

Overlap between the fentanyl market and the cocaine market appears to remain limited even as law enforcement across the country report more instances of the two drugs mixed. Two of the states with the most fentanyl reports in NFLIS in 2017—Ohio and New York—also overlapped with states that submitted the most cocaine reports, with Ohio overlapping between fentanyl, heroin, and cocaine. This may be due to a combination of the overall increased availability of cocaine in the United States and the significant co-occurrence of cocaine and fentanyl in overdose deaths.

Fentanyl represented nearly three-quarters of all state reports of fentanyl, synthetic opioids, and precursor chemicals to NFLIS in 2017, showing continued higher availability of the drug compared to other synthetic opioids (see Figure 4). Carfentanil was the second most reported synthetic opioid overtaking furanyl fentanyl (third), suggesting carfentanil availability increased between 2016 and 2017. Carfentanil's availability is largely driven by Ohio's submissions, which reported 77 percent of all state-level reports of carfentanil in 2017.

According to DEA's Fentanyl Signature Profiling Program (FSPP), fentanyl seized and analyzed in the United States in 2018 averaged 5.3 percent pure, based on analysis of approximately 722 fentanyl powder exhibits representing 929 kilograms. FSPP analysis indicated fentanyl available in the United States could range from 0.1 percent to 96.8 percent pure depending on

Figure 5. Fentanyl Combination Reports, 2014 – 2017



Source: DEA

DEA's Fentanyl Signature Profiling Program

The FSPP performs in-depth chemical analyses on fentanyl and fentanyl-related exhibits obtained from seizures made throughout the United States. Analytical methodologies developed at the Special Testing and Research Laboratory (STRL) give in-depth reporting on seizures and link seizures for intelligence purposes. FSPP data is not intended to reflect U.S. market share but, rather, is a snapshot of samples submitted to STRL from DEA regional laboratories.

A new methodology recently developed by DEA researchers can now routinely identify the fentanyl synthetic route (>65 percent of current samples). The previous methodology could only determine the route in approximately one percent of samples examined.

the source of the fentanyl. DEA and Customs and Border Protection (CBP) reporting indicates the fentanyl shipped directly from China is typically seized in smaller quantities with purities commonly testing above 90 percent. By comparison, fentanyl trafficked overland into the United States from Mexico is typically seized in larger, bulk quantities with much lower purity, with exhibits on average testing at less than ten percent pure. DEA's FSPP reported wholesale (typically ≥ 1 kg) fentanyl/heroin seizures accounted for approximately 16 percent by weight of the powders examined. Across all exhibits, fentanyl was mixed with heroin in 32 percent of the exhibits examined; indicating drug trafficking organizations (DTOs) at the regional and retail levels inside the United States are primarily responsible for the mixing of heroin and fentanyl rather than TCOs in Mexico.

According to NFLIS data, in 2017, fentanyl was most commonly observed as the only controlled substance in fentanyl exhibits tested by forensic

Fentanyl Resembling Black Tar Heroin Identified in Tucson

In August 2018, Tucson Police Department (PD) officers arrested an individual in possession of two individually wrapped bindles, one containing .75 grams of methamphetamine and the other containing .52 grams of a dark tar-like substance with a vinegar odor. The Arizona High Intensity Drug Trafficking Area (HIDTA) Counter Narcotics Alliance Task Force submitted both substances to the Tucson PD Crime Laboratory for analysis and identified that the black tar substance was fentanyl, most likely mixed with sugar. Although there have been seizures of fentanyl mixed with black tar heroin, this is the first known submission to the Tucson PD Crime Laboratory of fentanyl made to resemble black tar heroin. For context, in CY 2018, out of 1,283 total fentanyl exhibits, STRL analyzed 14 exhibits of "black tar" fentanyl. Of those, five contained heroin.

Figure 6. Fentanyl Resembling Black Tar Heroin

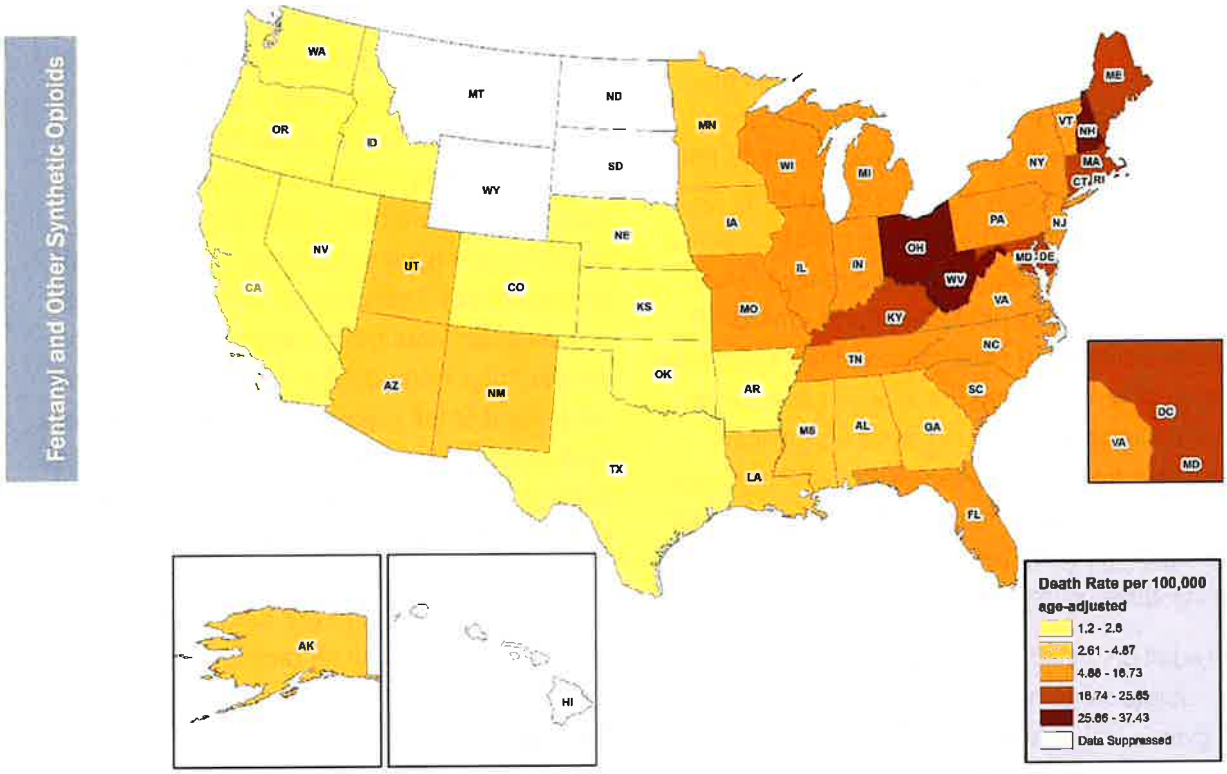
Source: Arizona High Intensity Drug Trafficking Area

laboratories across the country, continuing the trend of the past several years. Fentanyl with heroin was the most commonly observed mixture, with over nine times as many fentanyl and heroin mixtures identified as fentanyl and cocaine mixtures (see Figure 5). Between 2016 and 2017, the number of reports of fentanyl and heroin increased 97 percent; the number of reports of fentanyl and cocaine increased 74 percent; and the number of reports of fentanyl with methamphetamine increased 173 percent.

Use

Fentanyl use remains high in the United States and is a major contributor to the ongoing epidemic of drug overdose deaths. The high potency and powerful effects of fentanyl continue to cause users to overdose and die in record high numbers. The Centers for Disease Control and Prevention (CDC) reported a 47 percent increase in synthetic opioid-involved deaths from 19,413 deaths in 2016 to 28,466 deaths in 2017. Synthetic opioids were present in more drug-involved overdose deaths than any other illicit drug for the second consecutive year. While other substances, such as tramadol, are included in the synthetic opioid category, fentanyl is chiefly responsible for the synthetic opioid-involved deaths reported in this category. Fentanyl-involved overdose deaths continue to be highest in the Great Lakes, Midwest, and Northeast regions of the United States (see Figure 7). In 2017, West Virginia, Ohio, New Hampshire, Maryland, and Massachusetts

Figure 7. Synthetic Opioid-involved Deaths by State, Age-Adjusted Rate, 2017



Source: Centers for Disease Control and Prevention

had the highest age-adjusted rates of fentanyl-involved overdose deaths.

Fentanyl-containing counterfeit pills continue to be associated with overdose deaths across the country. Fentanyl traffickers use fentanyl powder and pill presses to produce pills that resemble popular prescription opioids, such as oxycodone and hydrocodone, and other popular prescription drugs, such as alprazolam. According to research from The Partnership for Safe Medicines (PSM), as of January 2019, 46 states[f] had encountered fentanyl-containing counterfeit pills since 2015. PSM reported that fentanyl-containing counterfeit pills were responsible for overdose deaths in at least 29[g] of those states. In many cases, the colorings, markings, and shape of the counterfeit CPDs were consistent with authentic prescription medications, meaning users might not be able to differentiate fentanyl-containing pills from authentic prescription medications.

- *In February 2019, Tucson, AZ Police responded to reports of multiple individuals overdosing at a party after taking fentanyl-containing counterfeit oxycodone pills. Police administered naloxone to the individuals, with treatment saving three people but coming too late for one person who died. Investigators believe the four thought they were taking authentic oxycodone and were unprepared for a dose of fentanyl.*
- *In March 2019, public safety officials in Minnesota said fentanyl pills disguised as oxycodone have appeared and may have caused the death of someone in the state. According to the Blue Earth County Sheriff's*

f. According to PSM, the only states with no confirmed presence of fentanyl-containing counterfeit pills were Delaware, Hawaii, Kansas, and Nebraska.

g. According to PSM, states with confirmed fatalities because of fentanyl-containing counterfeit pills were as follows: Arizona, California, Colorado, Connecticut, Florida, Georgia, Idaho, Illinois, Indiana, Iowa, Kentucky, Maryland, Mississippi, Montana, Nevada, New Hampshire, New Mexico, New York, North Carolina, Ohio, Oklahoma, Oregon, Pennsylvania, South Carolina, Tennessee, Texas, Utah, Virginia, and Washington.

Office, the decedent was found with blue "M30" pills, which investigators believe originated from drug traffickers in Mexico.

The inconsistent amount of fentanyl present in fentanyl-containing pills is another major contributor to pills' lethality. In 2018, DEA's FSPP examined 148 tablet exhibits representing 180 kilograms, in which the average tablet contained 1.5 milligrams of fentanyl with a range of 0.02 to 4.84 milligrams per tablet. Furthermore, 19 tablet exhibits (13 percent) contained a potential lethal dose of fentanyl (i.e. a dose greater than two milligrams). This represents a significant increase from 2017, when DEA's FSPP analyzed 72 exhibits representing 23 kilograms, of which seven exhibits (10 percent) contained potentially lethal doses of fentanyl.

In addition, in 2018, FSPP reported an increase in tablets containing acetaminophen and dipyrone, substances typically observed in Mexico-sourced heroin. To date, 85 exhibits (59 percent) contained a combination of acetaminophen and dipyrone as the primary diluents compared to only 17 percent of exhibits containing these substances in 2017. All of these tablets contained fentanyl HCl at an average dose of 1.6 milligrams per tablet with a range of fentanyl concentration from 0.5 to 2.3 milligrams per tablet. The consistency in the scientific profile of these counterfeit pills as well as the inclusion of substances commonly associated with Mexico-sourced heroin both indicate this particular "brand" of counterfeit tablet is likely produced by Mexican TCOs.

Production

Illicit fentanyl production requires no plant material; rather, it is synthesized in laboratories entirely from chemicals, unlike heroin. The fentanyl available in the United States is primarily sourced to either China or Mexico; however, there are new source and transit countries emerging as important players in the fentanyl threat. There are two primary methods to synthesize fentanyl: the Janssen method and the Siegfried method. DEA's STRL identified that 94 percent of the reports analyzed in 2018 were synthesized using the Janssen method versus six percent synthesized using the Siegfried method. The Janssen method is the more complex of the two methods of synthesis, indicating DTOs producing fentanyl are recruiting trained chemists to assist with fentanyl synthesis.

Transportation and Distribution

Traffickers smuggle fentanyl into the United States both by land, using the SWB, and by air, using international mail and express consignment carriers. Typically, fentanyl trafficked across the SWB is sourced to Mexico and fentanyl trafficked through the mail is sourced to China. Although DEA cannot geo-source fentanyl like heroin and cocaine, fentanyl trafficked into the United States from these two sources is distinct, allowing law enforcement to make a determination about origin. Fentanyl trafficked across the SWB from Mexico is typified by large volumes that are low in purity (less than 10 percent pure on average). Conversely, fentanyl trafficked through the mail from China typically arrives in smaller quantities that are highly pure (frequently 90 percent or higher purity).

Counterfeit Fentanyl Pill Mill Laboratory Seizures in Mexico

In 2018, Mexican law enforcement seized and dismantled two separate clandestine fentanyl pill-milling operations, one of which was allegedly responsible for producing carfentanil-laced counterfeit pills. The seizure of two separate counterfeit fentanyl pill milling operations in 2018 indicates Mexican TCOs are expanding their involvement in the trafficking of fentanyl by increasing the production of counterfeit fentanyl pills.

In September 2018, Mexican authorities located and secured the first suspected clandestine carfentanil pill milling operation in Mexico in the border city of Mexicali. A Bulgarian biochemist and his Mexican co-conspirator—both allegedly associated with the Sinaloa Cartel—were arrested during the operation. The dismantling of this lab resulted in the seizure of 20,000 suspected counterfeit carfentanil pills and a pill press. The Bulgarian biochemist is also accused, along with a second Mexican national associate, of conspiring to distribute carfentanil throughout the United States.

In December 2018, Mexican law enforcement seized a suspected fentanyl counterfeit pill mill in Azcapotzalco, Mexico City and arrested four individuals. Mexican officials seized suspected fentanyl-laced oxycodone M-30 pills, suspected fentanyl powder, precursor chemicals, and multiple items related to the production of fentanyl-laced counterfeit pills including one industrial press machine.

Given the differences in trafficking patterns, seizure amounts, seizure purities, and a lack of a distinct geographic forensic profile, it is currently not possible to identify whether China or Mexico is the primary fentanyl supplier to the United States. Seizures originating in Mexico represent a significantly larger total gross weight of fentanyl seized in the United States compared to fentanyl originating in China. However, the low purity of Mexico-sourced fentanyl means a relatively small portion of a given fentanyl seizure is actually fentanyl as opposed to other adulterants and diluents. DEA reporting also indicates Mexican traffickers order finished fentanyl from China, dilute it, and smuggle it into the United States. This means an unknown quantity of seized Mexican shipments of fentanyl were ultimately synthesized in China.

Mexico-Sourced Fentanyl

Mexican TCOs continue trafficking fentanyl in multi-kilogram quantities commingled with other drug shipments across the SWB. These TCOs combine fentanyl with diluents in clandestine facilities in Mexico prior to moving the drugs to the SWB region. According to CBP and DEA reporting, fentanyl mixtures with other illicit drugs are relatively uncommon at the wholesale level, meaning the mixing of fentanyl with heroin and other illicit drugs takes place inside the United States, not in Mexico. This indicates the mixing of fentanyl with other illicit drugs is not representative of an overall strategy by Mexican TCOs.

According to CBP data, 681 kilograms of fentanyl were seized along the SWB in 2018. This represents a 26.2 percent decrease from the 923 kilograms seized in 2017. The majority of fentanyl seized along the SWB was seized in California (75.7 percent) with Arizona second at 20.2 percent.

Mexico-sourced Counterfeit Oxycodone Pervasive in Sacramento Market

In April 2018, the Sacramento District Office (DO) seized more than 15,000 counterfeit generic oxycodone pills stamped with "M30" in Yuba City, California. These counterfeit pills were likely produced in Mexico. Later in June 2018, the Sacramento DO obtained more than 5,000 counterfeit generic oxycodone pills stamped with "M30" in Stockton, CA, likely sourced to Mexico. During September and October 2018, the Sacramento DO obtained more than 1,000 counterfeit generic oxycodone pills stamped with "M30" in Oroville, CA, also likely sourced to Mexico. Forensic laboratory testing confirmed the presence of fentanyl in all of the pill exhibits. This represents a shift in the production and distribution of counterfeit pills in the Sacramento DO area of responsibility (AOR). Historically, counterfeit pills were produced locally by DTOs; however, the last time the Sacramento DO seized a pill press was in October 2017.

Figure 8. Counterfeit M30 Oxycodone Pills Containing Fentanyl

Source: DEA

DEA reporting continues to indicate the Sinaloa and CJNG Cartels are likely the primary trafficking groups responsible for smuggling fentanyl into the United States from Mexico. To date, the fentanyl synthesis and fentanyl pill production operations dismantled in Mexico have occurred in Sinaloa-controlled territory. These TCOs are known to control the trafficking corridors in Mexico that connect to California and Arizona, meaning drugs passing through associated *locales* or plazas would need to be approved by these organizations. The use of poly-drug loads to smuggle multiple types of drugs across the border, a common tactic for fentanyl, is also typical of the Sinaloa and CJNG cartels.

Dominican traffickers, who are heavily involved in fentanyl trafficking in the Northeastern United States, are sourcing their fentanyl, both in powder and in pill form, from Mexican traffickers, expanding the reach of both organizations. U.S.-based Dominican Drug Trafficking Organizations (DTOs), supplied with fentanyl powder by Mexican TCOs, distribute both powder fentanyl and counterfeit fentanyl-containing pills to customers.

- *In December 2018, Boston's Organized Crime Drug Enforcement Task Force (OCDETF) Strike Force agents arrested two members of a Dominican DTO and seized approximately 1,300 grams of fentanyl. Subsequent to the arrest, agents obtained a search warrant for the source of supply's stash location in Massachusetts resulting in the arrests of two more defendants and the seizure of an additional nine kilograms of fentanyl and 3,000 counterfeit fentanyl pills.*
- *In January 2019, members of the New York FD and Homeland Security Investigations – Immigration and Customs Enforcement (HSI-ICE) executed an arrest warrant for a suspected money launderer involved with a Dominican DTO operating between Mexico, the Dominican Republic, New York City, and the Boston area that was supplying local residents with heroin and fentanyl. A consent search of the residence resulted in the seizure of approximately two kilograms of suspected heroin and fentanyl, approximately $100,000 United States Currency (USC), a kilogram press, eight bags of kilogram brick branding/marking stamps, and the components of a large heroin mill.*

- *In March 2019, the Boston Task Force working alongside the Boston, MA; Braintree, MA; Cambridge, MA; and Randolph, MA PDs and the Suffolk County District Attorney's Office executed several enforcement activities against a Dominican DTO operating in the area. Several motor vehicle stops and the execution of seven search warrants resulted in six arrests, the seizure of approximately $110,000 USC, two kilograms of suspected fentanyl, 200 grams of suspected cocaine, one vehicle, and one loaded firearm.*

China-Sourced Fentanyl

Fentanyl seizures in the international mail and express consignment operations (ECO) environments decreased significantly between CY 2017 and CY 2018, as did the percentage of seizures originating from China[h]. Total fentanyl seizures from the international mail and ECO environments declined by approximately 54 percent between 2017 and 2018, from 162.13 kilograms to 74.78 kilograms. Similarly, the total amount of fentanyl seized originating from China decreased 57 percent during the same timeframe, from 69.77 kilograms to 30.28 kilograms. In both 2017 and 2018, China was the single largest country of origin for fentanyl seized in the mail and ECO environments. Fentanyl originating from China represented approximately 40 percent of all seizures from the mail and ECO environments in 2018 compared to 43 percent of all international mail and ECO seizures in 2017. The cause of the substantial decrease in fentanyl seizures in the mail and ECO environments is yet unknown; however, contributing factors may include increased regulations in China on fentanyl and fentanyl-related substances[i] (FRSs), multiple high-profile successful dark web/open web operations, shippers' use of intermediary transit countries to disguise packages' origin, and Mexican TCOs' increasing production and trafficking of fentanyl.

- *In July 2018, the Atlanta FD identified a dark web vendor who used Chinese skincare products to conceal shipments of fentanyl smuggled into the United States from China. DEA, working in conjunction*

China Announces Controls on Fentanyl-Related Substances (FRSs)

On April 1, 2019, China announced it would control FRSs as a class effective May 1, 2019. China's new regulation defines an FRS as structurally related to (N-phenyl-N-[1-(2-phenylethyl) piperidin-4-yl] propanamide) by one or more of the following modifications:

- *Replacement of the N-propionyl group by another acyl group;*
- *Replacement of the N-phenyl group with any aromatic monocycle whether or not further substituted in or on the aromatic monocycle;*
- *Substitution in or on the piperidine ring with alkyl, alkenyl, alkoxyl, ester, ether, hydroxyl, halo, haloalkyl, amino or nitro groups; and/or*
- *Replacement of the phenethyl group with another group (exclude hydrogen atom)*

Officials from three Chinese agencies, including the Ministry of Public Security, announced the change at a news conference that included representatives from foreign embassies, including the American Embassy. The new restrictions will prevent drug traffickers from circumventing the law by changing fentanyl's formula to create FRS that are similar but not previously controlled. Further, the deputy director of the National Narcotics Control Commission stated Chinese authorities will urge courier companies to implement real-name registration for parcels and are increasing customs checks for high-risk international packages and further enhancing enforcement co-operation.

h. For the purposes of this data, seizures with a country of origin of Hong Kong were treated the same as seizures with a country of origin of China.
i. Fentanyl-related substances are substances in the fentanyl chemical family, but have minor variations in chemical structure (e.g., acetyl fentanyl, furanyl fentanyl, carfentanil).

with the United States Postal Inspection Service (USPIS), identified a package shipped from Sichuan, China, via an international mail service, which was supplied by the identified vendor. Law enforcement believed the package contained two grams of fentanyl, while the shipping label of the package stated the contents were cosmetic facial masks. Upon inspecting the package, law enforcement determined the presence of fentanyl inside a black box within the package that contained numerous individual packets containing facial masks. The fentanyl was discovered concealed inside a gel pack that would have contained a facial mask (see Figure 9).

Figure 9. Fentanyl Concealed in Gel Pack

Source: DEA

Pill Press Operations

Law enforcement across the United States continues to identify and dismantle more clandestine fentanyl pill pressing operations. These operations are popular since traffickers can invest in as little as a kilogram of fentanyl powder and produce hundreds of thousands of counterfeit fentanyl-containing pills to generate large amounts of revenue. Domestic clandestine pill press operators usually purchase already synthesized fentanyl and FRS in powder form, in addition to pill presses available from China, to create counterfeit pills intended for street sales. DEA and CBP must electronically approve the importation of tabulating/encapsulating machines. However, traffickers circumvent U.S. law by intentionally mislabeling shipments containing pill press parts and/or misrepresenting shipments on official customs forms. Moreover, there is no regulatory oversight of the machines after they enter the United States.

- *In October 2018 and January 2019, the Phoenix FD made significant seizures of counterfeit fentanyl-containing pills, highlighting the push by Mexican TCOs to produce and supply customers consistently with a fentanyl product besides powder fentanyl. In October 2018, the Phoenix FD seized approximately 30,000 "M30" counterfeit fentanyl-containing pills delivered by two couriers travelling on a shuttle van from San Luis, Arizona to Phoenix, Arizona. In January 2019, the Phoenix FD, in conjunction with United States Border Patrol (USBP), identified a juvenile drug courier operating in Yuma County, Arizona. The courier was stopped at the USBP checkpoint resulting in the seizure of 16 pounds of "M30" counterfeit fentanyl-containing tablets.*

- *Between July 2018 and August 2018, the Pittsburgh DO— in coordination with the Pittsburgh Bureau of Police— executed search warrants on two locations discovered to be pill press operations, seizing three pill presses. DEA indicated a single organization operated all three pill presses and produced counterfeit "M30" oxycodone tablets containing fentanyl and heroin. Law enforcement also seized heroin and fentanyl (dyed green and blue in color), weapons, and pill press dies at one of the residences. At the second residence, law enforcement seized five kilograms of "Firma Press" binding agent, three digital scales, beakers, grinders, and sifters (see Figure 10).*

Figure 10. Pill Press Equipment Seized in Pittsburgh, Pennsylvania

Source: DEA

India as an Emerging Source Country for Fentanyl

In late 2018, India emerged as a source country for fentanyl and fentanyl precursors trafficked by Mexican TCOs. DEA reporting identified a partnership between an Indian national and a Chinese national who worked in concert to obtain fentanyl precursor chemicals and fentanyl. The operation started in China but moved to India after the targets encountered difficulties obtaining precursor chemicals in China, possibly a consequence of China's previously announced regulations on fentanyl precursors 4-anilino-N-phenethyl-4-piperidone (4-ANPP) and N-phenethyl-4-piperidone (NPP). This may help TCOs to offset new regulations put in place by China, the primary supplier of FRS to the United States and fentanyl precursor chemicals to Mexican TCOs, if the regulations prove effective.

In the last half of 2018, DEA, in conjunction with Indian law enforcement authorities, conducted two separate operations that seized approximately 100 kilograms of suspected fentanyl or fentanyl precursors and 11 kilograms of fentanyl connected to an illicit fentanyl laboratory. Law enforcement reporting indicates the fentanyl in both seizures was intended for Mexican TCOs, indicating these groups are expanding their sources of supply beyond China. These investigations indicate Indian chemists have the knowledge and expertise to manufacture fentanyl without NPP and 4-ANPP, which will increase the difficulty of detection and oversight within India and throughout the international community.

- *In March 2019, the Phoenix FD Strike Force 2 working with the Tempe PD identified a DTO target expecting several fentanyl shipments from multiple couriers. DEA and local law enforcement identified a suspicious vehicle and conducted a traffic stop, which lead to a consensual search of the vehicle and the seizure of 6,000 counterfeit fentanyl-containing pills. Shortly afterwards, law enforcement located the DTO target at a Phoenix-area hotel and, after a consensual search of the premises, seized 19,000 fentanyl pills, $10,000 USC and two handguns.*

Outlook

Fentanyl will remain a serious threat to the United States as record numbers of individuals suffer fatal overdoses from illicit fentanyl sourced to foreign clandestine production. Clandestine fentanyl pill pressing operations will likely increase as DTOs seek to appeal to the large pill abuser population in the United States, with counterfeit fentanyl-containing pills continuing to be associated with clusters of overdoses and deaths due to inconsistent mixing and often unexpectedly high potency. The primary sources of fentanyl production and supply will likely shift as drug traffickers in other countries, such as India and Mexico, respond to China's new fentanyl legislation by expanding their own production and trafficking operations. Mexican TCOs will continue to serve as the suppliers of wholesale quantities of fentanyl to DTOs across the United States; whereas smaller, independent trafficking organizations will continue purchasing fentanyl from China on the open web and selling the drugs domestically on the dark web.

dea.gov/galleries/drug-images/fentanyl

Apps Relativity Suggested Sites

Fentanyl

Image 4 of 17, Date photo taken: 07/02/2018

photo illustration of 2 milligrams of fentanyl, a lethal dose in most people

Download Image

8

Indirect Methods to Estimate Prevalence

Matthew Hickman and Colin Taylor

MATTHEW HICKMAN • Imperial College
COLIN TAYLOR • European Monitoring Centre for Drugs and Drug Addiction

1. OVERVIEW

The first point to be made is that there are very good reasons to estimate the prevalence of problem drug use—which in this chapter refers almost exclusively to injecting drug use, heroin/opiate, and crack-cocaine use. The second is that population or general household surveys, which usually represent the best direct method of prevalence estimation, are not the answer for estimating these forms of problem drug use. Injecting drug users and opiate/ crack-cocaine users are comparatively rare and a largely "hidden" population—that is, they are hard to access by the usual means and are not readily accessed through surveys or administrative records. Counting the number of problem drug users in contact with treatment, police or other services is not sufficient as a prevalence estimate, since only a proportion of the target population is in contact with these services at any time and there is no available base or denominator.

Indirect methods offer an alternative way of estimating prevalence; some of these have been borrowed from animal ecology and some also are in use for other public health problems. In general indirect methods utilize routinely collected data sources. The discussion below presents examples of their use for estimating the prevalence of injecting drug use. The key to improving the evidence on the prevalence of problem drug use centers on improving the routine collection and integration of data on problem drug users that have as a goal "prevalence estimation".

1.1. Why Estimate Prevalence?

There is a growing recognition that policy-makers require evidence on the national and local prevalence of the problem. Gone are the days when, in response to one of the earliest attempts to estimate the prevalence of heroin use in the United States, a reviewer commented, "why bother estimating incidence and prevalence—would policy be any different if [there were] 300,000 or 3 million". (Hunt, 1974; Rittenhouse et al. 1997). Though some doubt whether policy is sufficiently evidence based, the growth in manuals on how to estimate prevalence and examples of prevalence estimates in support of policy is testament to the interest and importance of providing good evidence on prevalence (See, for example, Hser et al., 1992; GAP, 2002; EMCDDA, 1997, 2000; Hickman et al., 2003; Maxwell, 2000).

Prevalence estimates are required primarily in three key areas, service planning and resource allocation, monitoring key targets, and public health surveillance/epidemiology.

1.1.1. Service Planning and Resource Allocation

The prevalence of a disease can be central to arguments for securing resources for an appropriate response in terms of treatment and other measures to reduce

the associated harm. While it is the consequent public health and social problems associated with drug use that are directly or indirectly addressed, it is the overall level of prevalence that is frequently highlighted as a summary measure of these problems.

1.1.2. Monitoring Key Targets

The prevalence of problem drug use is often a component of local or national measures of the "coverage" of treatment or harm reduction. For example, in the United Kingdom the government is monitoring the proportion of problem drug users in contact with treatment. Globally, countries have been asked to estimate and monitor the proportion of injecting drug users in contact with services that seek to prevent Human Immunodeficiency Virus (HIV) infection.

1.1.3. Public Health Surveillance/Epidemiology

Prevalence estimates assist the interpretation and measurement of harms associated with drug use. The burden of HIV, Hepatitis C Virus, fatal overdose, and drug related crime associated with drug use in the population as a whole is related both to the level of risk behaviors found among problem drug users and to the prevalence of problem drug use itself. For example, the attributable risk fraction of mortality that may be caused by injecting/opiate use on adult mortality can be estimated by combining information on the prevalence of injecting/opiate use in the population and the Standardized Mortality Ratio of drug related mortality compared to the general population. (Bargagli et al., forthcoming)

Traditionally, the prevalence of an important public health problem would be one of the outputs of a public health surveillance system. The most common modern definition of "public health surveillance" is "the ongoing systematic collection, analysis, and interpretation of data on specific health events for use in the planning, implementation, and evaluation of public health programs" (CDC, 1988); often paraphrased as "information for action". (CDC, 1992). Public health surveillance systems for many infectious diseases are well established, and in developing countries have been extended to chronic diseases. Drug addiction was mentioned as a likely candidate for surveillance in 1968 (Berkelman and Buehler, 1991) though little work has been done to outline what a surveillance system for "drug addiction" would entail. We will come back to the principles of public health surveillance in the concluding section.

1.2. Why Indirect and Not Direct?

Direct methods for estimating levels of any behavior in a population (e.g. population or household surveys) are often considered a 'gold standard' for measuring prevalence, and they can be very effective in monitoring common drug

using behaviors such as tobacco or alcohol. However, direct methods are inefficient and ineffective when measuring the prevalence of rare, more covert, more stigmatized and more problematic forms of drug use, such as injecting or heroin or crack-cocaine use (NRC, 2001). Therefore there are multiple opportunities for bias. For instance, injecting drug users (IDU) or crack-cocaine users are less likely than non-problematic drug users to live in households included in general household surveys; IDU/crack users may be less likely to participate in the survey even if asked; and injection or crack use may be less likely to be reported than other forms of drug use.

Two studies illustrate these points. First, an analysis of combined surveys of over 90,000 subjects in the United States which presented cases by year of initiation failed to detect any change in the incidence of heroin use between 1960 and 1990—which is highly unlikely to be an accurate picture of use over that time period. (Gfroerer and Brodsky, 1992). Second, the 2001 British Crime Survey, with a sample size of over 30,000 found less than 50 people reporting that they used heroin in the last month, giving an estimate for Britain of 33,000, which is implausible as it falls short of the number of heroin users presenting to treatment sites (Aust et al., 2002).

Equally ineffective is an alternative strategy of compiling a register of known injecting drug users or crack-cocaine users. This is a common response in the monitoring of several diseases such as cancers, AIDS, Congenital Heart Defect, other congenital disorders, and childhood diabetes, but such an approach even if it combined multiple data sources would substantially under-estimate the prevalence of problem drug use. In theory, it is possible to ascertain a complete reporting of *all* diagnosed cases of diabetes or AIDS. However, in any one year a substantial proportion of problem drug users will not be in contact with *any* service so that a contact report could be made. In fact, it is not known what proportion of users over their injecting life-course will *not* have any contact with services.

2. INDIRECT ESTIMATION METHODS

The rationale for indirect estimation methods is that direct methods are impracticable or unreliable, and a simple count of known cases or instances will not suffice. In the absence of a ready-made sampling frame that covers problem drug users (PDU), the classical starting-point for direct methods, investigators turn to other means (Suzman et al., 1988). Animal ecologists face the same problem wanting to know the number or abundance of a specific animal in an area. As a result a number of indirect methods, appropriate to different animals and habitats, have been developed in ecology (Seber, 1982). The parallels between animal ecologists and epidemiologists (both estimating "elusive" and "hidden" populations) seems ready-made for injecting drug use and often have been noted, especially given

Table 1. Potential Data Sources for Indirect Estimation Methods

Data Source	Example
Specialist drug treatment	Drug users on methadone, attending treatment agencies, or in residential care
Low threshold drug agencies	Drug users attending drop-in sites or contacted by out-reach workers
Needle exchange	Drug users registered at needle exchange program (SEP)
Casualty	Drug users attending casualty because of an overdose or other problem
Laboratory	Drug users tested for HIV, HCV or HBV
Police/Prison	Drug users arrested or imprisoned for drug offences, Drug users arrested or imprisoned for other crimes but screened for drug problems
Probation	Drug users on probation
Social services—assessments	Drug users assessed by local social services
Hostels for drug users	Drug users living in hostels
Addict Registers	Drug users reported to a central register
Overdose deaths	Number of deaths due to opiate overdose

the widespread use of capture-recapture methods. However, we caution against reading too much into the parallel, since normally the conduct of the studies and the statistical models are very different.

The starting point for indirect estimation is having data on a sample of problem drug users (referred to as the observed data set), which though may be partial provides some information on the characteristics and number of problem drug users. The aim of the indirect estimation methods is to analyze the observed data set or combine it with other information to estimate the "proportion of the [problem drug use] target population sampled within the observed data set", and thereby to arrive at an estimate of the prevalence. Table 1 shows some potential data sources used in prevalence estimation, some of which may be available locally or could be generated.

Indirect methods use these data sources as their raw material and seek to estimate the sampling intensity, i.e. the proportion of the total number of problem drug users sampled in the study. Often this requires having sufficient information on the data sources to match against subjects who appear on two or more data sources; or to obtain other information on how a specific data source (in Table 1) relates to the overall population of problem drug users. The question of this approach then is whether multiple data sources or samples can be used to ascertain the proportion of subjects observed or not observed at a particular source. In this problem of 'incomplete ascertainment' over multiple data sources, it is important to explicitly recognize that many subjects (problem drug users) are unknown to any one or all of the data sources. The disadvantage of indirect methods is that a series of assumptions are made regarding the relationship of the observed data

set(s) to the numbers of problem drug users in the target population (these are summarized below). Furthermore, violation of the assumptions may lead to bias so that the precision of the estimates or how accurately the model represents the target population cannot be empirically tested. Table 2 summarizes a number of indirect estimation methods.

Therefore the central problem in designing indirect estimation studies is obtaining a random sample of problem drug users in first instance. While it is relatively easy in direct estimation methods to check that a sample has been drawn from the sampling frame in a random manner, at least in so far as the design has been properly operationalized, it is far more difficult to make a similar assessment when using indirect methods. A range of assumptions is required that in essence ensure two things: firstly, that the sample behaves, in statistical terms, as though drawn from a conceptual (but unattainable) sampling frame; and secondly, that the required design procedures are operationally valid (i.e., correctly identifies the sample and its relationship with the total population).

These assumptions (some or all of which apply to the various indirect methods) include the following: having a stable population, having equal probabilities that a single subject will be observed in a given data source, matching of subject characteristics can be made across data sources, and that appearing on a data source is independent of appearing on others.

1. Stability of Population: The number of drug users entering or exiting from the population over the period of study is negligible in practical terms. Technically, if the 'time spent at risk of being observed' is known, then corrections can be made to allow for a shifting population—but in practice, this is never the case.

2. Equi-probable sampling: There is an equal probability of any subject being observed at a given data source. Technically, where multiple data sources are used, this requirement need apply only to one of the sources.

3. Matching definitions: Definitions of groups of subjects and the identification of individual subjects should match correctly across data sources. Technically, this implies no misclassification of subjects as IDU or PDU, or false negative or positive matches of subjects between data sources.

4. Source conditional independence: If a subject appears on one data source he/she is not more or less likely to appear on another data source, i.e., positive or negative dependence. Technically, in ecology studies it refers to trap fascination or trap avoidance, or significant interactions in statistical parlance. In theory dependence can be adjusted for in the analysis, except if in a study of n data sources where there are n-way interactions. For example, with two samples the data sources must be independent, with three data sources there must be no 3-way interaction and so on.

In practice, all the methods presume that the data sources are broadly representative of the population being studied, or at least aim for that as the safest design. It has been noted (Cormack,1992) that in contrast to direct estimation there

Table 2. Indirect Methods of Estimating Prevalence of Injection/Problem Drug Use (IDU/PDU)

Method	Summary	Example
Multiplier methods	Combines data on number of known IDU (benchmark, eg, number in treatment, tested for HIV, fatal OD) and information on proportion of IDU that would appear on benchmark (multiplier, e.g proportion in treatment, tested for HIV, died of fatal OD) to estimate total IDU population.	See Archibald (2001), Hartnoll (1985)
Capture-recapture methods	Takes and matches 3 or more data sources of IDU (eg. Treatment, arrest, syringe exchange), analyses the overlap between the data sources using log-linear models to estimate the number of IDU "unobserved" by the data sets and the total number of IDU	See Hook and Regal (1995), Hickman (2004)
Capture-recapture methods—open populations	Analyses repeat captures/surveys over time (e.g. number of occassions sex workers observed over time, or re-attendances by IDU at injecting room) to estimate total population size and its rate of change over time	See McGeganey (1992)
Truncated Poisson	Takes single data source (e.g. attendances at treatment, arrests, visitis to SEP) and analyses frequency of 1, 2, etc attendances in order to probability of attending once, twice etcc and predict probability and proportion of subjects attending 0 times, and estimate total IDU population.	See Hay (2003)
Enhanced/event Based multipliers	Collects data on event history from multiple data sources/benchmarks (e.g. history of imprisonment, treatment, hostel use), combines them in order to adjust for biases, and combines them with benchmarks to estimate total number of IDU/PDU	See Simeone (1997)
Synthetic estimation	Takes estimates of IDU population in selected sites (usually generated by other indirect methods) and estimates number of IDU in other sites using proportional ratio or regression methods based on single or multiple indicators of IDU that are available in all areas (e.g. number of fatal OD, drug treatment and criminal justice data).	See Rhodes (1993), Frischer (2001)
Back-calculation	Uses information on trends in an observed end-point (e.g. fatal OD), combined with information on the incubation distribution (e.g. heroin/1DU cessation rate, OD and drug related mortality rate) to estimate incidence and prevalence of heroin/1DU use) over time.	See Law (2001), De Angelis (In press)

are no clear sample size calculations that can be made in advance of an analysis that could guarantee a level of reliability. Though as a general rule the greater the amount of data collected and the greater the sampling intensity the better (Wittes 1974). Furthermore, though some methods can generate confidence intervals using standard statistical equations, any uncertainty (or bias) arising from sampling the population is often far outweighed by uncertainty or bias arising from violation of the assumptions and uncertainty surrounding some of the data inputs. It is rarely possible to test empirically whether the final prevalence estimates are true. For this reason it is essential that the estimates are "evidence based" i.e. that the estimates are corroborated or consistent with other information, or other knowledge and expertise is used to help judge whether the estimates are credible. The methods generally used to make indirect prevalence estimates include: multiplier methods, capture-recapture, and others. The following sections discuss each of these methods, offering case studies as examples of their application.

2.1. Multiplier Methods

Multiplier methods (also referred to as ratio-estimation) were probably the first and most common methods for estimating the prevalence of problem drug use. Superficially versatile, easy to use and calculate, in theory they can use any of the data sources given in Table 1. Two elements are required: first, a data source usually called a "benchmark" (representing a known number of problem drug users that have experienced a particular event, such as treatment or arrest or overdose); second, an estimate of the proportion of all problem drug users that have been recorded in the benchmark (e.g. the proportion in treatment might be 1 in 10; or 1 in 50 arrested, or overdose mortality rate amongst problem users might be 1 in 100). The reciprocal of the proportion is termed the multiplier. The benchmark represents the known drug users and the proportion estimates the 'sampling intensity' that generated them. For example, if the benchmark were 3,000 and it was estimated that 20 percent of the population under investigation were recorded on the benchmark, the multiplier would be 5 (since 1/20percent = 5) and the estimated total would be calculated as 15,000 (that is, 5 * 3,000).

In essence, the multiplier is a two-source method (one source is the benchmark, the other is the data used to provide the estimate of the proportion and multiplier). The assumptions of the multiplier method are all those outlined above, i.e., the population of problem drug users needs to be stable and the same during the benchmark recording as during the multiplier estimation; the sample that is used to estimate the multiplier should be representative of the overall population of problem drug users, in practice not easily done; and, it is important that the definition used for the benchmark is precise and matches exactly that used in estimating the multiplier. As an example of this latter point, if arrest data are used for the benchmark then the multiplier needs to find the proportion of drug users arrested,

not those charged or sentenced. Or again, if a number of treatment clinics' records over one year is the benchmark, then the multiplier must relate to attendance at those clinics over that year.

In the 1970s, mortality multipliers were used to estimate the prevalence of opiate use in the United States and United Kingdom (Andima et al., 1973; Hartnoll et al., 1985). For example, Hartnoll et al. (1985) multiplied the annual number of opiate overdose deaths by 50 to 100 on the basis that opiate overdose mortality rate was 1 percent to 2 percent per annum. Multiplier methods also have been applied to arrest data, treatment statistics and HIV reports (see box), and these methods continue to be used (Archibald et al., 2001; Frank et al., 1978; Parker et al., 1988; Godfrey et al., 2002; Dupont, 1973; Hall, 2000).

Various methods have been used to derive the multiplier, all attempting to approximate a random sample of drug users from which to estimate it. These include—not always successfully—site sampling methods (sampling drug users present at a representative set of geographical sites), and 'community sampling' (chain referral or snowball techniques that attempt to produce a representative sample of all drug users).

Nomination also has been used to obtain a multiplier (Parker et al., 1988). This describes a technique where a sample (e.g. injecting drug users) are asked questions about their friends or acquaintances (their nominees) that also are injecting drug users. For example, Parker and colleagues conducted a study with sixty IDU in the Wirral who were asked to nominate their five closest acquaintances and say how many were in treatment last year. The sixty IDU reported 300 other IDU. After removing duplicates this figure was reduced to 170 of whom 55 were identified as being in treatment giving a proportion of 32.4 percent and a multiplier of 3.1 (Parker et al., 1988).

Case Study 1 conducted by Archibald and colleagues (2001) for Toronto used as a benchmark laboratory reports of HIV test results that indicated injecting drug use as a risk factor and a survey of injectors from several Canadian cities asked

Case Study 1. Multiplier Study Based on HIV Tests in Toronto

Benchmark (B)	Number of HIV tests by injecting drug users in 1996—*Source: laboratory reports*	4050
Multiplier (M)	Proportion of injectors reporting getting an HIV test in the previous year—*Source: community recruited survey of injectors*	23% (multiplier = 1/0.23 = 4.35
Prevalence estimate	B * M (4050*4.35)	17,600

about being tested for HIV in the same year as the multiplier. In addition to showing how the multiplier method is applied, this example also illustrates the underlying problems with this approach:

- Is the benchmark complete and accurate? It may be necessary to adjust the benchmark, for example, to account for missing exposure information and/or HIV tests.
- Is the multiplier representative of the target population? This presents a greater problem. In this case study information from a community sample of IDUs recruited in a different year and city was used to derive the multiplier. Ideally, the multiplier should be obtained from a representative sample of problem drug users and collected over the time period and place corresponding to the benchmark data. In practice, however, random and representative samples of IDU are nigh on impractical to obtain.

Great caution needs to be exercised when using multiplier studies that are not confirmed, validated, or cross-checked with other information and other studies.

2.2. Capture Recapture

Capture-recapture methods were developed by animal ecologists to estimate animal abundance and the dynamics of animal populations (Begon, 1979). There are two principal types of model: closed and open population models. Open population models relax assumption #1(having a stable population) and because of the need for multiple independent data sets have had limited use in estimating the prevalence of problem drug use (see the two examples below). Closed population models with two data sources are more vulnerable to assumption #4 (having independent data sources) than those with three or more data sources, as it is not possible to test the independence of the two samples in the analysis.

Capture-recapture methods have been used extensively in epidemiology to adjust surveys, surveillance systems, and disease registers for under-ascertainment and therefore to estimate prevalence. (Chandra Sekar et al., 1949; Fienberg, 1992; Hook and Regal, 1995; International Working Group for Disease Monitoring and Forecasting, 1995). Bishop et al (1975) were the first to identify the potential for capture- recapture methods in estimating the prevalence of addiction, which since have been used in many cities worldwide (Hickman et al., 1999, 2004; Hay and McKegany, 1996; Squires et al., 1995; Hay, 2000; Brugha et al., 1998; Domingo-Salvaney et al., 1998, 1995; Bello and Chene, 1997; Kehoe et al., 1992; Comiskey and Barry, 2001; Duque-Portugal et al, 1994; Larson et al., 1994).

Ideally, capture-recapture involves the collection of three or more data sources of problem drug users with sufficient detail on the subjects to identify matches between data sources. Information on the number of matches between the data

Case Study 2a. Estimating Number of Injecting Drug Users in Bangkok, 1991

		Arrestees with urine positive for opiates (S2) Yes	No	
Methadone Maintenance (S1)	Yes	171	3893	4064
	No	1369	?(x)	
		1540		N

So,

population estimate, $N = n_1, * n_2 / m = 4064 * 1540 / 171 = 36{,}599$

number observed, $n, = a + b + c = 171 + 3893 + 1369 = 5433$

hidden, $x, = N - n$, or, $c * b / a = 36{,}599 - 5433$ or $1369 * 3893 / 171 = 31{,}166$

95%c.i. $= 1.96 * \sqrt{(n_1, * n_2 * b * c)/m^3} = 1.96 * \sqrt{(1540 * 4064 * 3893 * 1369)/171^3} = 4516$

Rounded Estimate of IU in Bangkok in 1991 = 36,600 (32,000 to 40,800)

KEY

a or m = marks, number of people in both S1 and S2

b = number in S1 but not S2

c = number in S2 but not in S1

x = hidden population, number of people not in S1 or S2

n_1 = number of people in S1

n_2 = number of people in S2

N = total population

sources (i.e., the number of people that occur in more than one data source) is used to estimate the sampling intensity (i.e., the total proportion of injectors in the samples). These estimates of the number unobserved are then combined with the number in the data sources to generate the overall prevalence estimate. Studies with two samples can be easily calculated (see below). Those with three, four or more samples require statistical packages (such as STATA or GLIM or SPSS) as the data are analyzed using log-linear models with dependencies (technically, 'interactions') between data sources to generate an adjusted prevalence estimate. The following references give an essential background to the methods and their use in epidemiology (Hook and Regal, 1995; International Working Group for Disease Monitoring and Forecasting, 1995).

Case study 2a shows an example by Mastro and colleagues (1994) who carried out a two sample study in Bangkok in 1991. They collected two samples, 4064 heroin users in methadone treatment and 1540 people that had been arrested and tested positive for opiates. There were 171 people on both lists giving an estimate of 36,600 opiate users (0.5 percent of total population) in Bangkok in 1991.

Case Study 2b. Multi-data source Capture-recapture Study of Prevalence of IDU in Brighton, UK, 2001

Contingency Table—showing number of subjects matched between data sources

Brighton		Treatment							
		Yes				No			
		Arrest Referral							
		Yes		No		Yes		No	
		Survey & A&E							
		Yes	No	Yes	No	Yes	No	Yes	No
Syringe	Yes	1	8	7	65	3	19	36	521
Exchange	No	2	7	6	103	2	42	74	

Data sources:

Specialist Drug Treatment	Arrest Referral	Survey & A&E	Syringe Exchange	Total records	Total Individuals	Matched	
199	84	131	660	1074	896	156	17%

Prevalence estimate:

population (15–44)	observed	estimate of unobserved	Total number IDU (95% CI)		Prevalence (95% CI)	
117,032	*896*	*1,408*	*2,304*	*1514–3737*	*2.0%*	*1.3–3.2%*

Model Selection:

Interactions: treatment*arrest referral, treatment *syringe exchange, arrest referral*survey_a&e syringe exchange*survey_a&e G^2 11.81, p-value 0.98, degrees of freedom 24

The problem with the two-sample study is that it is not known whether the two data sources (police and treatment) are independent (assumption #4). If not, and the proportion of the population captured or observed in the data sources is low (1 in 7 in the Bangkok study) then the potential for error is large (Wittes et al., 1974).

In a study in Brighton four data sources were analyzed (specialist drug treatment, criminal justice, syringe exchange, and community survey). The box (above) shows the contingency table, summary of the data sources, prevalence estimates and the best fitting model. The contingency table, instead of a 2 *2 as in the Bangkok study, shows the number of subjects across all four data sources. The number unobserved in the last cell with a "." represents those cases that do not appear on any of the data sources. In total 156 subjects (17 percent) were on more than one data source and one person was on all four data sources. The analysis suggested that the best model identified complex interactions between the data sources, making the basic analyses difficult and less reliable than if only a simple model was required for the data. The prevalence estimate itself could be considered high at 2 percent among adults aged 15–44. The authors note that compared to many capture-recapture studies for drug use the estimated number and proportion of

unobserved subjects is comparatively low (i.e., ~900 : 1400, 1 : 1.5); that the capture-recapture estimate was lower than for a mortality multiplier estimate; and that local policy-makers were consulted and agreed that the estimate was consistent with other available information.

We should note here that complex dependency models can result from heterogeneity among the subjects (violation of assumption #2). Heterogeneity is often regarded as inevitable when using health data (Hook and Regal, 1995) as there are many examples of differences in health seeking behaviors and arrests by gender, age-group, social class, ethnic group, and degree of dependence. To avoid or limit the influence of these factors, analyses are made by first stratifying the data into more homogeneous subsets of people that are analyzed separately (for example, fitting separate models for males and females or by age group). Alternatively, covariate capture-recapture techniques have been developed that allow fewer models to be fitted including both dependencies between data sources and those potentially between covariates (e.g., by gender and age-group) (Tilling and Sterne, 1999).

Two other assumptions that were potentially violated in this and many capture-recapture studies are *misclassification* bias (assumption #3) and closed population (assumption #1). Often there is insufficient information in the data sources to identify matching individuals; moreover subjects may give pseudonyms to different data sources to protect their identity. Studies would benefit by estimating the misclassification error thus allowing sensitivity tests of the robustness of the estimates (as animal ecology studies allow for loss of marks).

A *closed population* (i.e., no deaths, new cases, cessation or migration) is clearly an impossibility, but the bias of using an open capture-recapture method can be limited if the study time interval is short in comparison to the life cycle of the subject (e.g., a year for an injecting drug user may not be too serious a bias and allows sufficient data to be gathered to identify matches). Alternatively, open capture-recapture models seek to estimate population prevalence and change over time. However, there are very few examples of this approach in the epidemiological literature. One such study estimated the prevalence of street sex workers in Glasgow (McKeganey et al., 1992) through fieldwork over a succession of nights. They built "capture-histories" of women (e.g., on how many nights they were observed). The study suggested that the number of sex workers on the street remained approximately the same over a year but that the population of sex workers changed at approximately 8 percent per week. A new study by Kimber and colleagues used attendance histories at a safe injecting room to estimate prevalence over time (Jo Kimber, personal communication). This type of application is rare as there are hardly any single data sources that could meet assumption #2, requiring the data source to be representative of the target population. Pollack (1990) proposed mixed closed and open models as an answer to problems of heterogeneity, dependence, and dynamic populations, which may prove interesting to pilot in drug abuse.

2.3. Other Indirect Methods

Multiplier and capture-recapture estimates are the most common indirect prevalence methods used for problem drug use. Below, we mention other methods, some more recent in their development: truncated poisson, synthetic estimation, back calculation, and enhanced/event based multipliers.

2.3.1. Truncated Poisson

Truncated Poisson methods use information on repeat events to estimate the size of the population with 0 events. All the assumptions above apply, however, the strength of two of these assumptions and the availability of data limit its use. For instance, the assumption that repeat events are independent, i.e., that a person arrested or in treatment once is as likely to be re-arrested or re-enter treatment as someone who has not yet been "captured"; and the assumption that *all* subjects are as likely as each other to generate an event are easily violated. Also, as in the case of open capture-recapture models, the problem is to find a single data source that is representative of problem drug users. Certainly, criminal justice or specialist drug treatment data alone are not sufficient. Hay and Smit (2003) demonstrated the potential of truncated poisson applied to injecting drug users attending a syringe exchange in Scotland, estimating from attendance records of 647 subjects in a city in Scotland that there were a total of 1041 injectors.

2.3.2. Synthetic Estimation

Synthetic estimation or the multiple indicator method is a form of extrapolation (or technically 'regression on principal components'), which makes use of known prevalence figures in certain regions (that may have been estimated using multiplier or capture-recapture methods) to estimate prevalence in other regions. To do this correctly, these regions for which prevalence is being estimated must have data sources that are the same as (or very similar to) the regions for which prevalence estimates exist.

Extrapolation can be based on a single value, e.g., the proportion of opiate overdose deaths (Hall et al., 2000), or multiple indicators (Frischer 2001, Kraus 2003). It should be noted that there are some technical and statistical considerations that apply when more than one anchor point is used in a regression analysis, requiring discussion with an experienced statistician. For example, should a Poisson regression be used as opposed to using simple linear regression analysis and should rates or log-transformed data be used; should a weighting for the different anchor points be established to represent the reliability of the problem drug use prevalence estimate; and is the relationship between the drug indicator and the problem

drug use prevalence rates similar across all the data points and is the relationship between prevalence and indicators valid.

2.3.3. Back-calculation

Law and colleagues (2001), and De Angelis and colleagues (in press) adapted back-calculation methods to estimate the incidence and prevalence of heroin use. The back-calculation method developed in AIDS epidemiology is based on the relationship between the time of infection (the presence of HIV), the incubation time, and the development of the disease (the diagnosis of AIDS). Knowledge of any two of these three components allows estimation of the third. Typically, the distribution of the incubation time and the incidence of the end point are assumed known and the infection process underlying the observed incidence is estimated. The estimated infection process is then used with the same information on the incubation time to predict the incidence and prevalence of the end-point of interest. When used for drug abuse epidemiology the observed incidence of the end-point has generally been opiate overdose death, with trends over time provided by routine mortality statistics. The "incubation" distribution is the distribution of the time between starting and stopping injecting, where the stopping process is the result of either a fatal overdose or the actual cessation of injecting. The data demands are considerable including reliable mortality statistics to identify the number of opiate overdose deaths, data on the opiate overdose and other drug related mortality rates of injecting drug users, and information on the cessation rates from injecting.

2.3.4. Enhanced/Event Based Multipliers

Simeone and colleagues (1997) have suggested modifications to the simple multiplier. Instead of a single proportion as a multiplier, a detailed multiple event history using multiple data sources are collected, in order theoretically to adjust for the inherent biases present in any single data source. However, these methods have only been piloted and are not in general use.

3. CONCLUSIONS

This chapter presented the indirect methods currently being used to estimate the prevalence of drug abuse in various populations. We have been critical of these methods pointing out their limitations and that the estimates derived from them need to be interpreted with caution. However, we believe that they are the answer to the problem of estimating the prevalence of rare problem drug using behaviors such as the use of heroin, drug injecting, or crack-cocaine use as population

surveys are inefficient and not cost effective. Data sources for capture-recapture and multplier estimates should be carefully chosen to minimize both dependence and heterogeneity. Most communities have data that are available and these can be assessed for their utility for prevalence estimation. For example, do the data sources collect data on drug profile (injecting status, and problem drugs), collect identifiers to allow matching with other data sources /or/ if anonymised suffer little under-reporting; would problem drug users remember or recognise being captured by the data source, are only a sub-set of problem drug users captured by the data source; is it known how the data sources relate to other potential data sources. If the available data sources are poor—recommend steps to policy-makers (and data owners) to improve them for future estimation work. Collecting the data is the most time consuming part of prevalence estimation work. This work could be dramatically reduced if contributing to prevalence estimates was one of the objectives of routine data on problem drug use—such that a "public health surveillance" system of problem drug use was developed that specifically linked and integrated multiple data sources to allow prevalence estimation.

Finally, multiplier and capture-recapture estimation methods tend to be more reliable within discrete geographical locations in part to avoid heterogeneity (i.e., the relationship between the population of problem drug users and data sources is likely to vary from city to city), which has implications for public health surveillance and the design of studies.

REFERENCES

Andima, H., Krug, D., Bergner, L., Patrick, S., and Whitman, S. (1973). A prevalence estimation model of narcotics addiction in New York City. *American Journal of Epidemiology* 98, pp. 56–62.

Archibald, C.P., Jayaraman,G.C., Major, C., Patrick, D.M., Houston, S.M., and Sutherland, D. (2001). Estimating the size of hard-to-reach populations: a novel method using HIV testing data compared to other methods. *AIDS* 15 (suppl3), pp. S41–48.

Aust, R., Sharp, C. and Goulden C. (2002). *Prevalence of drug use: Key findings from the 2001/2002 British Crime Survey. Findings 182* Home Office Research, Development and Statistics Directorate, London, England.

Bargagli AM, Hickman M, Davoli M, Perucci CA, Schifano P, Buster M, Brugal T, Vicente J. (Forthcoming) Drug related mortality and its impact on adult mortality in eight European countries.

Begon, M. (1979). *Investigating Animal Abundance- Capture-Recapture for Biologists*. Edward Arnold, London, England.

Bello, P.Y. and Chene, G. (1997). A capture-recapture study to estimate the size of the addict population in Toulouse, France. In: European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). *Scientific Monograph Series No. 1. Estimating the Prevalence of Problem Drug Use in Europe.* EMCDDA, Lisbon, Portugal, pp. 91–103.

Berkelman RL, Buehler JW. (1991) Surveillance. Chapter 11 pp. 161–176 In: Holland WW, Detels R, Knox G. (Eds.), Oxford Textbook of Public Health. 2nd Edition. Volume 2. Oxford: OUP.

Bishop, Y.M.M., Fienberg, S.E. and Holland, P.W. (1975). *Discrete Multivariate Analysis: Theory and Practice*. MIT Press, Cambridge, Massachusetts, US.

Brugha, R., Swan, A.V., Hayhurst, G.K., and Fallon, M.P. (1998). A drug misuser prevalence study in a rural English district. *European Journal of Public Health* 8, pp. 34–36.

Centers for Disease Control. (1988). *Guidelines for evaluating surveillance systems*. MMWR 37, p. S5.

Centers for Disease Control. (1992). *Proceedings of the 1992 International Symposium on Public Health Surveillance*. MMWR 41 Supplement, pp. 1–218.

Chandra Sekar C, Edwards Deming W. (1949). On a method of estimating birth and death rates and the extent of registration. *American Statistical Association Journal* pp. 101–115.

Comiskey, C.M. and Barry, J.M. (2001). A capture-recapture study of the prevalence and implications of opiate use in Dublin. *European Journal of Public Health* 11(2), pp.198–200.

Cormack, R.M. (1999). Problems with using capture-recapture in epidemiology: An example of a measles epidemic. *Journal of Clinical Epidemiology* 52, pp. 909–914.

De Angelis, D., Hickman, M., and Yang, S. (In press). Estimating long-term trends in the incidence and prevalence of opiate/injecting drug use and the number of ex-users: The use of back-calculation methods and opiate overdose deaths. *American Journal of Epidemiology.*

Domingo-Salvany, A., Hartnoll, R.L., Maguire, A., Brugal, M.T., Albertin, P., Cayla, J.A., Casabona, J. and Suelves, J.M. (1998). Analytical considerations in the use of capture-recapture to estimate prevalence: Case studies of the estimation of opiate use in the metropolitan area of Barcelona, Spain. *American Journal of Epidemiology* 148(8), pp. 732–740.

Domingo-Salvany, A., Hartnoll, R.L., Maguire, A., Suelves, J.M. and Anto, J.M. (1995). Use of capture-recapture to estimate the prevalence of opiate addiction in Barcelona, Spain, 1989. *American Journal of Epidemiology* 141, pp. 567–574.

Dupont, R.L. and Piemme, T.E. (1973). Estimation of the number of narcotic addicts in an urban area. *Medical Annals of the District of Columbia* 42, pp. 323–326.

Duque-Portugal, F., Martin, A. J., Taylor, R. and Ross, M.W. (1994). Mark-recapture estimates of injecting drug users in Sydney. *Australian Journal of Public Health* 18, pp. 201–204.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). (1997). *Scientific Monograph Series No. 1. Estimating the Prevalence of Problem Drug Use in Europe.* EMCDDA, Lisbon, Portugal.

European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). (2000). *EMCDDA Recommended Draft Technical Tools and Guidelines—Key Epidemiological Indicator: Prevalence Of Problem Drug Use*. EMCDDA, Lisbon, Portugal. Available at: http://www.emcdda.org/situation/themes/problem_drug_use.shtml.

Fienberg, S.E. (1992). Bibliography on capture-recapture modelling with application to census undercount adjustment. *Surveillance Methodology* 18, pp. 143–154.

Frank, B., Schmeidler, J., Johnson, B. and Lipton, D.S. (1978). Seeking truth in heroin indicators: the case of New York City. *Drug and Alcohol Dependence* 3, pp. 345–358.

Frischer, M., Hickman, M., Kraus, L., Mariani, F. and Wiessing, L. (2001). Comparison of different methods for estimating the prevalence of problematic drug misuse in Great Britain. *Addiction.* 96: 1465–1476.

GAP Toolkit Module 3. (2002). *Prevalence Estimation—Indirect Methods for Estimating the Size of the Drug Problem.* UNDCP, Vienna, Austria. (Editors: Taylor C. Hickman M.).

Gfroerer, J. and Brodsky, M. (1992). The incidence of illicit drug use in the United States, 1962–1989. *British Journal of Addiction* 87, pp. 1345–1351.

Godfrey, C., Eaton, G., McDougall, C. and Culyer, A. (2002). *The Economic and Social Costs of Class A Drug Use in England and Wales, 2000.* Home Office Research Study 249. Home Office Research, Development and Statistics Directorate, London, England.

Hall, W., Ross, J., Lynskey, M., Law, M. and Degenhardt, L. (2000). How many dependent heroin users are there in Australia? *Medical Journal of Australia* 173, pp. 528–531.

Hartnoll, R., Lewis, R., Mitcheson, M. and Bryer, S. (1985). Estimating the prevalence of opioid dependence. *The Lancet* 1(8422), pp. 203–205.

Hay, G. (2000). Capture-recapture estimates of drug misuse in urban and non-urban settings in the north east of Scotland. *Addiction* 95, pp. 1795–1803.

Hay, G. and Smit, F. (2003). Estimating the number of drug injectors from needle exchange data. *Addiction Research and Theory* 11, pp. 235–243.

Hay, G. and McKegany, N. (1996). Estimating the prevalence of drug misuse in Dundee, Scotland: an application of capture-recapture methods. *Journal of Epidemiology and Community Health* 50, pp. 469–472.

Hickman, M., Stimson, G., Howe, S., Farrell, M., Taylor, C., Cox, S., Harvey, J., Frischer, M. and Tilling, K. (1999). Estimating the prevalence of problem drug use in inner-London: A discussion of three capture-recapture studies. *Addiction* 94, pp. 1653–1662.

Hickman M, Taylor C, Chatterjee A, Degenhardt L, Frischer M, Hay G, Tilling K. (2003). Estimating drug prevalence: Review of methods with special reference to developing countries. *UN Bulletin on Narcotics*; LIV (1 and 2), pp. 15–32.

Hickman M., Higgins V., Hope V., Bellis M., Tilling K., Walker A., Henry J. (2004). Injecting drug use in Brighton, Liverpool, and London: best estimates of prevalence and coverage of public health indicators. *Journal of Epidemiology and Community Health* 58(9), pp. 766–771.

Hook, E.B. and Regal, R.R. (1995). Capture recapture methods in epidemiology: Methods and limitations. *Epidemiologic Reviews* 17, pp. 243–264.

Hser, Y-I., Anglin, M.D., Wickens, T.D., Brecht, M.L. and Homer, J. (1992). Techniques for the Estimation of Illicit Drug Use. *Prevalence: An Overview of Relevant Issues*. National Institute of Justice, Washington, D.C.

Hunt, L.G. (1977). Recent spread of heroin use in the United States. *American Journal of Public Health* 64, pp. 16–23.

International Working Group for Disease Monitoring and Forecasting. (1995). Capture-recapture and multiple record systems estimation I: History and theoretical development. *American Journal of Epidemiology* 142, pp. 1047–1057.

Kehoe, L., Hall, W. and Mant, A. (1992). Estimates of the number of injecting drug users in a defined area. *Australian Journal of Public Health* 16, pp. 232–237.

Kraus L., Augustin R., Frisher M., Kummler P., Uhl A., Wiessing L. (2003). Estimating prevalence of problem drug use at national level in countries of the European Union and Norway. *Addiction* 98, pp. 471–485.

Larson, A., Stevens, A., and Wardlaw, G. (1994). Indirect estimates of "hidden" populations: Capture-recapture methods to estimate the numbers of heroin users in the Australian Capital Territory. *Social Science and Medicine* 39, pp. 823–831.

Law, M., Lynskey, M., Ross, J. and Hall, W. (2001). Back-projection estimates of the number of dependent heroin users in Australia. *Addiction* 96, pp. 433–443.

Lynskey, M., Degenhardt, L., Law, M.G., Ross, J. and Hall, W. (In press). Capture-recapture estimates of the number of individuals who are heroin dependent in New South Wales, Australia. *Substance Use and Misuse.*

Mastro, T.D., Kitayaporn, D., Weniger, B.G., Vanichseni, S., Laosunthron, V., Thongchai, U., Uneklabh, V., Vhoopanya, K. and Kimpakarnjanarat, K. (1994). Estimating the number of HIV-infected injection drug users in Bangkok: a capture-recapture method. *American Journal of Public Health* 84, pp. 1094–1099.

Maxwell, J.C. (2000). Methods for estimating the number of hard core drug users. *Substance Use and Misuse* 35, pp. 399–420.

McKeganey, N., Barnard, M., Leyland, A., Coote, I. and Follet, E. (1992). Female streetworking prostitution and HIV infection in Glasgow. *British Medical Journal* 305, pp. 801–804.

National Research Council. (2001). *Informing America's Policy on Illegal Drugs: What We Don't Know Keeps Hurting US*. Editors, Manski C., Pepper J., Petrie C. National Academy Press, Washington, D.C.

Parker, H., Bakx, K. and Newcombe R. (1988). *Living with Heroin*. Milton Keynes: Open University Press.

Pollack K.H., Nichols J.D., Brownie C., Hines J.E. (1990). Statistical inference for capture-recapture experiments, Wildlife Monographs, Wildlife Society, Department of Fisheries and Wildlife Sciencies, Virginia Polytechnic Institute and State University, Blacksburg, VA.

Rittenhouse, J.D. (Editor). (1977). *The Epidemiology of Heroin and Other Narcotics*. National Institute on Drug Abuse Research Monograph 16. National Institute on Drug Abuse, Rockville, Maryland.

Rhodes W. Synthetic estimation applied to the prevalence of drug use. (1993). *The Journal of Drug Issues* 23, pp. 297–321.

Seber, G.A.F. (1982). *The Estimation of Animal Abundance and Related Parameters*. 2nd Edition. Charles W Griffin, London, England.

Simeone, R., Rhodes, W., Hunt, D. and Truitt, L. (1997). *A Plan for Estimating the Number of "Hard-core" Drug Users in the United States*. Drug Policy Research Group, Office of National Drug Control Policy, Washington, D.C.

Squires, N.F., Beeching, N.J., Schlect, J.M. and Ruben, S.M. (1995). An estimate of the prevalence of drug misuse in Liverpool and a spatial analysis of known addiction. *Journal of Public Health and Medicine* 17(1), pp. 103–109.

Suzman, S., Sirken, M.G. and Cowan, C.D. (1988). Sampling rare and elusive populations. *Science* 240, pp. 991–996.

Tilling, K. and Sterne, J.A.C. (1999). Capture recapture models including covariate effects. *American Journal of Epidemiology* 149(4), pp. 392–400.

Wittes, J.T., Colton, T. and Sidel, V.W. (1974). Capture-recapture methods for assessing the completeness of case ascertainment when using multiple information sources. *Journal of Chronic Diseases* 27, pp. 25–36.